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SUBCLINICAL MITRAL DISEASE

CHAIRMAN'S ADDRESS

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BOSTON

Mitral stenosis is almost invariably acquired and is practically always the result of rheumatic fever. It is most frequently found between the ages of 15 and 40 and is more common in females than males by a ratio of three to two.

Mitral insufficiency may be either organic or relative. Relative mitral insufficiency is secondary to dilatation of the left ventricle, which may occur from a number of causes. Organic mitral insufficiency is also almost always the direct result of rheumatic fever. The former is of more serious import as it usually occurs in a dilated heart. Organic mitral insufficiency may exist for years without impairing the efficiency of the heart but often is followed by mitral stenosis or subacute bacterial endocarditis. Although mitral insufficiency may persist alone for many years, very commonly the signs of insufficiency disappear, stenosis develops or the patient may succumb to subacute bacterial endocarditis, an all too frequent eventuality.

From a study of the pathologic physiology consequent on mitral stenosis or mitral insufficiency it is evident that dilatation of the left auricle will almost invariably ensue in both conditions. It is reasonable to conclude, therefore, that careful roentgen study could be of help in the diagnosis of mitral disease by demonstrating the dilated left auricle. If mitral stenosis alone is present there will be no enlargement of the left ventricle. If, as much more frequently occurs, the stenosis is associated with mitral insufficiency, there will also be enlargement of the left ventricle.

The diagnosis of mitral stenosis can be made by several different methods, particularly auscultation, roentgen examination and electrocardiography. Other signs may suggest the presence of the condition or may contribute to the diagnosis but are rarely pathognomonic. The most widely used and the most accurate method is careful auscultation. In the early stages of the process the trained ear will hear a snapping first sound, which suggests the diagnosis, and a short presystolic or middiastolic rumbling murmur which is practically pathognomonic. It may be necessary to have the patient go through a short period of vigorous exercise to bring out the characteristic late diastolic rumble or it may be heard only when the patient is lying on the left side. In this stage it may easily be overlooked. In more advanced degrees of mitral stenosis the murmur may fill all of diastole and is more easily heard. Usually, of course, there is an accompanying systolic murmur.

The next most important method of confirming the diagnosis is the demonstration of the dilated left auricle fluoroscopically or roentgenographically. This is second in importance only to the characteristic diastolic murmur in the opinion of Parkinson.[1]

The third observation of critical importance is less frequent but may lead to the correct diagnosis in a doubtful case. This is the presence of a broad, flattened P wave in the electrocardiogram, especially if right axis deviation is also present. This should lead one to make a presumptive diagnosis of mitral stenosis even in the absence of the characteristic diastolic murmur, as in case 4.

The typical auscultatory observations may be absent or overlooked (*a*) in the early stages of the process, when the change in the diameter of the valve orifice is slight and the murmur absent or very faint, and (*b*) in the advanced stages of the process, particularly when there is heart failure. The velocity of the blood flow through the mitral valve produces the murmur, so that if there is great dilatation of the chambers the velocity may be quite slow and the murmur very faint or absent. In this type of heart the murmur may reappear as the failure disappears. This is particularly true when there is auricular fibrillation with heart failure.

In the great majority of the cases of mitral stenosis, roentgen examination will demonstrate dilatation of the left auricle. This is best seen in the right anterior oblique position and may be of sufficient degree to displace the esophagus posteriorly and sometimes to the patient's right. In the postero-anterior view the change in the cardiac contour may be less marked and less characteristic. There may be only a straightening of the normally concave "waist" of the heart on the left border, a contour not typical of mitral disease. In the more advanced cases the left contour presents the double convexity of the dilated pulmonary artery and tip of the dilated left auricle between the aortic knob and the left ventricular contour (figs. 1 and 2). Fluoroscopic examination is much more valuable in the study of heart disease than are x-ray films. The observer is better able to separate the different chambers by their alternate pulsations and can note abnormal pulsations. He may bring out changes in heart size and relations by different phases of respiration. More important still, he may select the best amount or degree of rotation to study the contours of the various chambers and vessels and may note the effect of changed contour on neighboring structures such as the esophagus. Fluoroscopy is the only reliable method of finding, locating and identifying areas of intracardiac calcification during life, a finding which may be of critical importance in the diagnosis.

The fluoroscopic examination of a patient with mitral valvular disease, therefore, should reveal: 1. A straightening or a double convexity of the midportion of the

Read before the Section on Radiology at the Ninety-First Annual Session of the American Medical Association, New York, June 13, 1940.

1. Parkinson, John: Enlargement of the Heart (Lumleian Lecture), Lancet **1**: 1337 (June 13), 1391 (June 20) 1936.

left cardiac contour. 2. Dilatation of the left auricle posteriorly, best shown in the right anterior oblique position. The convex curve of the dilated auricle is located in the middle third of the cardiac shadow and may obscure the middle third of the posterior mediastinal space. 3. Widening of the base of the heart in the right anterior oblique view, due to the combination of enlarged pulmonary conus anteriorly and dilated left auricle posteriorly.

Fluoroscopy may also show: 4. Displacement of the barium-filled esophagus posteriorly with moderate to marked dilatation of the auricle, best shown during the expiratory phase but most reliable when also present during inspiration. 5. Dilatation of the pulmonary vessels at the lung roots due to stasis in the pulmonary circulation. These vessels do not pulsate as in Ayerza's disease and patent ductus arteriosus. They may be considerably dilated and congested without producing physical signs or symptoms. 6. Hypertrophy of the right ventricle, seen best in the exaggerated left anterior oblique view, which reveals a ledge or shoulder projecting anteriorly. 7. Narrowing of the precardiac space in the lateral view, with a greater amount of the heart in contact with the sternum than normal and (8) a hypoplastic aortic knob, in cases in which the mitral stenosis was acquired in childhood. Marked dilatation of the pulmonary artery may partly obscure the aortic knob, making it seem hypoplastic by comparison. The real hypoplasia is thought to be due to a decreased volume of blood from the left ventricle, in turn due to the mitral stenosis.

In advanced or long standing mitral valvular disease, the left auricle may be so dilated that it will displace the left bronchus upward and may even compress it. This may result in dyspnea, cough, atelectasis or obstructive emphysema of the left upper lobe. In other advanced cases the left auricle may extend far to the right and make up a part or even all of the right cardiac contour, sometimes simulating the contour seen with tricuspid insufficiency. When a double contour on the right is seen, the upper convexity will be due to the left auricle, which will lie more posteriorly than the lower one. If the tube is shifted from side to side the upper curve will be seen to move in the opposite direction more than the lower one, indicating its more posterior position. This is the principle of parallax, used in locating metallic foreign bodies. Usually there is an easily perceptible difference in pulsation, the two chambers contracting and expanding alternately. This is due to the systolic expansion of the left auricle as a result of the mitral insufficiency. A dilated descending branch of the right pulmonary artery may simulate a dilated left auricle projecting to the right and may even show a transmitted systolic pulsation immediately following the auricular contraction of the lower (right auricular) convexity. The true character of this upper curve may be recognized by watching it carefully while rotating the patient to the left, and by noting the point of origin and the other branches of the artery on the film, where it is wedge shaped, base up.

Of these signs the dilated left auricle is the only important or critical one: the others are supportive and confirmatory. Of still greater value and, in my experience, absolutely pathognomic, is the demonstration of calcified areas in the mitral valve. Calcification in the injured mitral valve is found in the majority of cases at autopsy but is unfortunately not visible fluoroscopically in more than 10 per cent of the patients during life. This is in striking contrast to aortic stenosis, in which the majority will have deposits of calcium large enough to be readily demonstrable under the fluoroscope.[2]

These diagnostically important intracardiac deposits of calcification are easy to find and easy to differentiate if a few simple rules are followed. They are most easily located fluoroscopically. The observer's eyes must be thoroughly prepared by at least fifteen minutes in a completely darkened room. A radiolite wrist watch or a Pirie photometer can be used to test accommodation for night vision. With the eyes properly accommodated, the usual screen examination is carried out and then the observer narrows the fluoroscopic aperture to a few square centimeters and looks through the heart, searching for dark dancing shadows. The intracardiac calcium deposits all show a to and fro movement with systole and diastole, and those in the valves may have an excursion of 2 or 3 centimeters, sometimes in an elliptic or triangular course. The calcified aortic and mitral valves are found under a line along the auriculoventricular sulcus, which is usually about 45 degrees from the horizontal. The auriculoventricular junction is easily identified on the left border. The patient should be rotated slightly to the left, so that the calcified areas will not be hidden by the spine. The patient should take a deep inspiration and hold it, so that the underlying pulmonary markings will be immobile and not confusing. This also helps by intensifying the contrast due to the distention of the lung. If the heart has the "mitral" configuration, the calcified areas are nearer the apex than with the "aortic" configuration, where they are found nearer the base. This is due to the dominance of the dilated auricles in the first type of heart and of the hypertrophied ventricle in the "aortic" type. If a calcified valve is found a fairly accurate guess can be made as to which valve is calcified by considering the shape of the heart. A more reliable and more accurate means of differentiating between the calcified aortic and mitral valves is to rotate the patient to the opposite side (left anterior oblique), where the mitral valve will be found to be in the posterior third of the heart shadow, while the aortic valve will be found in the middle third. The pulmonic and tricuspid valves are very rarely calcified and do not enter into the differential diagnosis as a rule. A frequent source of error, however, is calcification of the mitral annulus fibrosus. This is frequently quite massive and is the most easily demonstrable of the three. However, the calcified annulus is usually either U shaped or J shaped or O shaped, and it is more homogeneous than the irregular mulberry-like calcification in the valves themselves. Its movements are similar to those of the calcified mitral valve but its clinical significance is nil. It occurs only as a senile change, usually in persons over 60 years of age, and is often associated with arcus senilis and calcification of the intervertebral disks. There is no dilatation of the left auricle with calcification of this ring, as the mitral valve is not involved and its function is not affected.

The other intracardiac calcifications are not ordinarily confused with calcification in the valves. Calcification large enough in amount to be visible fluoroscopically has been found in (*a*) the coronary arteries,[3] (*b*) the pericardium, (*c*) the myocardium, such as calcified infarcts, (*d*) the endocardium, particularly of the auri-

2. Sosman, M. C.: Roentgenological Aspects of Acquired Valvular Heart Disease, Am. J. Roentgenol. **42**: 47-56 (July) 1939.

3. Wosika, P. H., and Sosman, M. C.: The Roentgen Demonstration of Calcified Coronary Arteries in Living Subjects, J. A. M. A. **102**: 591 (Feb. 24) 1934.

cles, and (*e*) rarely in one of the benign tumors. The latter has not yet been found during life; the others have all been noted during life and subsequently confirmed at autopsy.

There is no special apparatus required to demonstrate these calcified valves, just the regular fluoroscope with a 5 inch gap, 5 milliamperes of current, a small fluoroscopic aperture and a screen of fine grain and high intensity like the type B fluoroscopic screen. The sensitization of the eyes for fifteen minutes is probably the most important step in the procedure.

If one finds, therefore, a dilated left auricle and calcification in the mitral valve, one can make an unequivocal diagnosis of mitral stenosis. The presence of calcification in the mitral valve indicates in my opinion the rheumatic etiology, as I have not found this degree of calcification in the mitral valve to be due to either syphilitic or atherosclerotic processes. I feel that this is true also in the majority of cases of aortic stenosis with calcification. If the appearances are those of a dilated left auricle with the collateral observations already noted and without demonstrable calcification of the mitral valve, the diagnosis of mitral stenosis is highly presumptive, even in the absence of other physical signs.

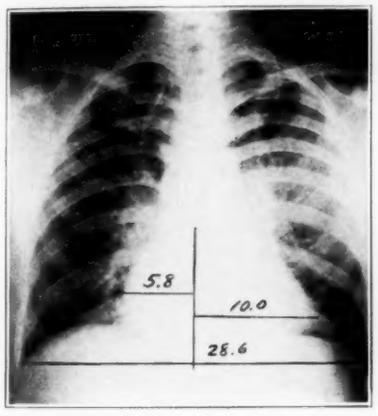

Fig. 1 (case 1).—Seven foot film of the heart showing general cardiac enlargement and the fulness in the middle third of the left cardiac contour very suggestive of mitral disease.

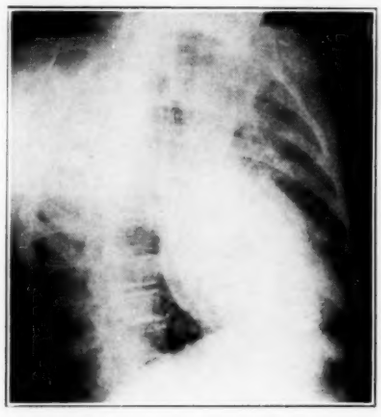

Fig. 2 (case 1).—Right anterior oblique film showing marked dilatation of the left auricle posteriorly, displacing the esophagus in a characteristic concavity, highly suggestive of mitral stenosis.

Fig. 3 (case 1).—Spot film taken at 30 inch distance, 200 milliamperes, one twentieth second, showing an irregular mass of calcification in the mitral valve (arrows), unequivocal evidence of mitral stenosis, and posterior displacement of esophagus (single arrow).

For many years my associates and I have regularly made a fluoroscopic examination of all patients sent to us for examination of the heart and nearly all of those sent for chest examination. In addition we make a fluoroscopic examination of the chest in all gastrointestinal examinations.

During this time, but more particularly since 1935 when we found an unsuspected mitral stenosis in one of our technical staff, we have recorded for purposes of investigation those clinically undiagnosed cases of mitral disease as "subclinical mitral disease." This is admittedly an erroneous and etymologically incorrect label. If strictly interpreted it could mean "mitral disease under the bed." What we do mean, I think, is amply explained by the preceding discussion, that is, patients with mitral disease whose condition was clinically undiagnosed before roentgen examination. We soon found that such patients could be grouped or classified in several subdivisions. For our own purposes of record we have termed them class A, B and C. The class A group is a small one. These patients have unequivocal roentgen signs of mitral disease, but the clinical observations are either absent or inconclusive. The diagnosis could not be made at the time of examination without the roentgen signs. Cases 1 and 2 reported herewith are typical examples of this group.

Class B is the largest group and includes the patients with undoubted mitral disease in whom the physical signs of the disease were overlooked by one or more competent physicians before the roentgen examination. The appearances by fluoroscopic and film examinations were quite definite, and careful study by our cardiologist, Dr. S. A. Levine, brought out the definite signs of mitral disease and confirmed the diagnosis. The diagnosis could have been made by the cardiologist without the roentgen examination. A third group, class C, includes those patients with the roentgen findings compatible with mitral disease but not characteristic of it and with no clinical or other observations to corroborate the diagnosis. Patients in this group are being followed to see if they subsequently develop typical clinical signs of mitral disease or other conditions to explain the abnormal roentgen appearances. No doubt we should add a fourth group, class D, to include those patients in whom the clinical signs of mitral disease are quite definite but the roentgen appearances are either inconclusive or negative. This group is quite small. Roesler[4] says that dense mediastinal adhesions may account for the lack of dilatation of the left auricle in those cases.

The list of conditions which may cause dilatation of the left auricle and thus simulate mitral disease is usually given as follows: Thyrotoxicosis, emphysema, pneumoconiosis, fibrosis of the left upper lobe, beriberi, congenital heart disease, especially patency of the ductus arteriosus and pulmonic stenosis, scoliosis of the spine to the right, and pleuropericardial adhesions. Tumors in the auricle close to the valve could of course cause mechanical stenosis of the valve and might in time give rise to the usual roentgen configuration of mitral disease.[5] In my experience most of the foregoing conditions either fail to simulate the appearance of mitral disease or do so only but rarely, particularly emphysema, pneumoconiosis, pulmonary fibrosis, scoliosis and extrapericardial adhesions. As to the others, thyrotoxicosis in my experience rarely causes changes in cardiac contour which would simulate mitral disease except in failing hearts with auricular fibrillation. Patent ductus

4. Roesler, Hugo: Clinical Roentgenology of the Cardiovascular System, Springfield, Ill., Charles C. Thomas, 1937, p. 193.

5. Wainwright, C. W.: Intracardiac Tumor Producing the Signs of Valvular Heart Disease, Bull. Johns Hopkins Hosp. **63**: 187-200 (Sept.) 1938.

arteriosus can and does simulate mitral disease roentgenographically and may cause dilatation of the left auricle as is reported by Eppinger and Burwell [6] in this symposium. Similarly it may give the clinical signs and murmurs of mitral disease, as occurred in one of the cases included in the report by Dr. Gross.[7] The most frequent cause of error in the diagnosis of mitral disease in our series is in heart failure from any cause, particularly with cardiac dilatation and auricular fibrillation. The dilated left auricle seen in these conditions may actually be due to relative mitral regurgitation or to stasis in the atonic fibrillating auricle. Sussman and Woodruff [8] have shown that fibrillation of the auricles is rarely followed by dilatation of the auricles unless complicated by valvular disease. As a matter of actual practice in fluoroscopic examination we rarely see patients with the degree of cardiac failure just noted, and those with thyrotoxicosis can usually be differentiated by the hyperactivity of the heart and by the absence of the normal sinus arrhythmia. Moderate degrees of left auricular dilatation may be present in ambulatory patients with heart failure due to nonvalvular lesions such as beriberi, anemia or nephritis, but in general I agree with Parkinson [1] that definite dilatation of the left auricle is one of the most certain signs of mitral stenosis, and this is particularly true in the absence of heart failure.

Fig. 4 (case 2).—Seven foot film of the heart showing general cardiac enlargement and the double convexity in the middle third of the left cardiac contour suggesting mitral stenosis.

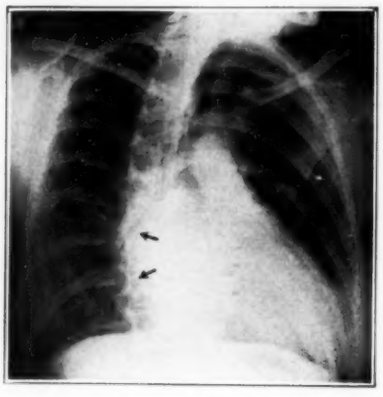

Fig. 5 (case 2).—Right anterior oblique film showing marked dilatation of the left auricle (arrows) projecting beyond the anterior border of the spine.

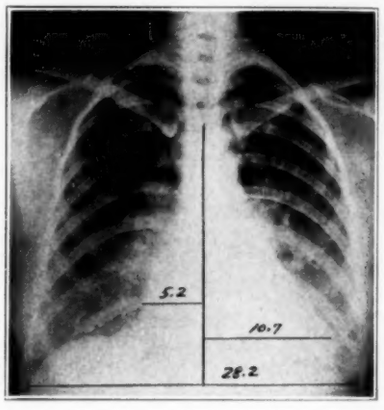

Fig. 6 (case 3).—Seven foot film of the heart showing slight cardiac enlargement, a straight left border without convexities, and fairly marked dilatation of the pulmonary vessels. Patient was symptomless at time.

The accuracy of our clinical diagnoses in acquired valvular heart disease is quite high, particularly in the hands of trained cardiologists, but most of these patients are in advanced stages of the disease and many are soon confirmed at autopsy. Our accuracy in the early stages of the disease is open to question, as there is often a long latent period between a given attack of rheumatic fever and the discovery of mitral stenosis. The process must inevitably have been present and gradually progressing during the latent period when no murmurs, or only a systolic murmur, were present. Mitral stenosis does not appear suddenly; it is a slow gradual process. It is quite possible, therefore, that the routine use of the fluoroscope by a trained observer may be of aid in the earlier diagnosis of mitral stenosis. There is little of therapeutic value in the earlier diagnosis of mitral stenosis as there would be in the early diagnosis of cancer or of pulmonary tuberculosis. The treatment would not be any different nor would it presumably have any different effect. The value of such studies must lie therefore in the difference in prognosis, with a possible change in our ideas as to the latent or inactive period in potential heart disease—that period between the first infection with rheumatic fever and the onset of symptoms or the discovery of physical signs of acquired valvular heart disease. The difficult differential diagnosis in this stage is between no heart disease at all with a normal prognosis and acquired mitral valvular disease, which is of quite serious import and which automatically carries with it a bad prognosis as to length of life.

REPORT OF CASES

CASE 1.—D. G., an Italian laborer aged 38, was first seen in the medical outdoor department of the Peter Bent Brigham Hospital on Oct. 7, 1938, complaining of shortness of breath on exertion for about one year, and epigastric pain, thought to be due to peptic ulcer. He was accordingly referred to us for gastrointestinal examination and during the routine fluoroscopy of his chest an enlarged heart of mitral configuration was noted (figs. 1 and 2). On looking through the heart with the fluoroscope, we found a calcified area in the region of the mitral valve (fig. 3) with the characteristic dancing movements during the cardiac cycle. The left auricle was dilated posteriorly and there was bilateral pulmonary congestion. Neither at that time nor subsequently in the cardiac clinic were physical signs of mitral stenosis heard, but Dr. Levine concurred in the diagnosis after seeing the x-rays and the report of fluoroscopy.

No history of rheumatic fever could be elicited, but he had suffered from frequent nosebleeds as a child—one of the stigmas commonly associated with rheumatic fever. The patient was studied thoroughly in the medical ward from Sept. 14 to Sept. 27, 1939, and again no definite diagnosis of mitral stenosis could be made except by roentgen examination.

Additional observations in the ward were noncontributory and are given here only for the sake of completeness. The urine was normal with a specific gravity varying from 1.012 to 1.016; no sugar or albumin was found. Blood examination showed hemoglobin 105 per cent, red blood cells 5,220,000, white blood cells 9,100, polymorphonuclears 75 per cent, hematocrit 42 per cent. The serologic reaction was negative. The phenolsulfonphthalein excretion was 70 per cent in two hours. Gastric analysis revealed hyperacidity. The spinal fluid was normal, including the colloidal gold curve, protein determinations and manometric readings. The icteric index was 5. The vital capacity was 2,300 cc. The basal metabolic rate was —8 per cent. The sedimentation rate was 30 mm. an hour. The venous pressure was 65 mm. of water. The circulation time (decholin

6. Eppinger, E. C., and Burwell, C. S.: The Mechanical Effects of Patent Ductus Arteriosus on the Heart and Their Relation to the X-Ray Signs, J. A. M. A., to be published.
7. Gross, R. E.: Experiences with Surgical Treatment in Ten Cases of Patent Ductus Arteriosus, J. A. M. A., to be published.
8. Sussman, M. L., and Woodruff, M. T.: Significance of Left Auricular Dilatation in Auricular Fibrillation, Am. J. Roentgenol. **40:** 184-188 (Aug.) 1938.

method) was 18 seconds. An electrocardiogram showed normal curves. Scratch sensitivity tests showed increased sensitivity to several materials. A gastrointestinal series was normal. Cholecystograms were normal. Dr. Romano, on analyzing the patient, found a rather profound psychoneurosis.

The patient has been seen several times since his discharge from the hospital, his condition essentially unchanged, with no definite signs or symptoms of cardiac disability except for the occasional paroxysmal and nocturnal attacks of dyspnea, which were thought not to be of cardiac origin. There was no improvement in his condition nor has there been any worsening. The last note on his record is the rather cryptic one that in the spring of this year (1940) he had borrowed $300 and returned to Italy, leaving his wife and children in Boston.

CASE 2.—R. D., a married woman aged 37, Jewish, was admitted to the hospital Jan. 11, 1936, because of pain in the right leg of three days' duration. Physical examination revealed an enlarged heart, with auricular fibrillation but no significant murmurs. Dr. Levine felt that she had an enlarged heart with auricular fibrillation and thought that she might have mitral valvular disease because of the presumed embolus to the right femoral artery and other episodes suggesting peripheral emboli. Roentgen examination (figs. 4 and 5) confirmed the suspicion of mitral stenosis, revealing fairly marked cardiac enlargement both to the right and to the left, with marked dilatation of the left auricle obscuring the posterior mediastinal space and displacing the esophagus backward and to the right. Pulmonary congestion was also present. No calcification of the mitral valve could be demonstrated but the diagnosis of mitral stenosis appeared to be quite definite without it. Dr. Levine stated that he could only suspect the presence of a mitral stenosis in the absence of the characteristic murmur, but with the roentgen observations the diagnosis seemed quite certain.

The patient's response to therapy was not satisfactory and she died in June 1936, presumably from a pulmonary infarction. Unfortunately an autopsy was not obtained.

These two patients are both listed in our records as class A: ones in whom the diagnosis of mitral stenosis could not be made without the roentgen examination. There are others in the same group, each presenting a particular problem of his own, but none any less definite than case 2 or more positive than case 1, in which we feel that the diagnosis of mitral stenosis is unequivocal in spite of absence of clinical signs and symptoms.

There are many more patients listed in class B but a detailed presentation of their vital statistics would be of no particular value to the informed reader. It is common knowledge that a particular diagnosis can be made more easily and more accurately by the man who

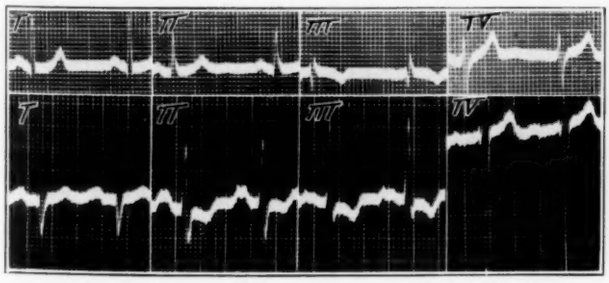

Fig. 7 (case 4).—Upper curves show electrocardiograms of a normal patient. Lower set clearly indicates mitral stenosis. Note prominent broad topped and notched P waves (lead 2) and right axis deviation.

has the most interest and the most experience in that field. There is no doubt that many cases of mitral stenosis are overlooked in their earlier stages; in fact there must be a stage in most of the cases in which the condition is still latent and the diagnosis cannot be made by any means. We can only speculate at present as to whether or not the left auricle is already beginning to dilate when the diastolic murmur first becomes audible. Additional work is being done along these lines.

As one example typical of the whole group of class B patients I cite case 3:

CASE 3.—H. R., an unmarried woman aged 36, a nurse technician, complained of ease of fatigue, loss of weight, shortness of breath on exertion and troublesome cough at times. Fearing pulmonary tuberculosis, she asked for an x-ray examination of her chest. We found (fig. 6) no evidence of primary pulmonary disease but we did note considerable pulmonary congestion chiefly around the hili and an abnormal contour of the heart shadow, with straightening of the left border, slight cardiac enlargement and definite dilatation of the left auricle posteriorly. No calcification of the mitral valve could be demonstrated, but we felt that the diagnosis of mitral stenosis was highly presumptive.

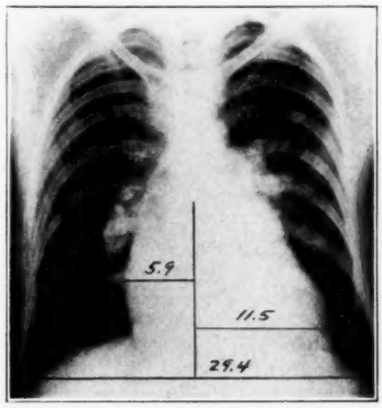

Fig. 8 (case 4).—Seven foot film of the heart showing marked cardiac enlargement both to the right and to the left, a double convexity on the left border and dilatation of the pulmonary vessels, suggesting combined valvular heart disease, primarily mitral.

A study of her past history revealed chorea at the age of 18, scarlet fever at the age of 19 and frequent attacks of tonsillitis during the past twelve years. She had been seen by several competent physicians in the past few years but they had not made the diagnosis of mitral stenosis. Dr. Levine, however, was able to detect the faint diastolic murmur characteristic of the disease and made the diagnosis without reservation. The patient had intermittent but progressive symptoms of cardiac failure during the succeeding three years and died in cardiac decompensation July 26, 1938. During her periods of decompensation the diastolic murmur would decrease in intensity and sometimes disappear.

CASE 4.—J. S. B., a man aged 33, was admitted to the hospital Jan. 16, 1940, in heart failure. There was no past history of rheumatic fever, but he had been told that he had heart murmur in childhood. He had suffered from shortness of breath for four years and had a series of small hemoptyses three years before admission. Following appendectomy one year before admission there were migratory joint pains which were considered to be due to rheumatic fever. Dr. Levine has seen the patient four years before, at which time he found a systolic murmur only, but he made a presumptive diagnosis of mitral stenosis because of the electrocardiographic tracings, which showed a broadened flattened P wave (fig. 7).

Physical examination on admission showed him to be in heart failure, fibrillating, with rales at both bases, fluid at the right base, moderate venous engorgement, slight pitting edema of the lower extremities and a markedly enlarged tender liver. The first sound at the apex was snapping in character; there was a grade 3 systolic murmur but no diastolic murmur could be heard.

X-ray examination (fig. 8) revealed marked cardiac enlargement, with marked dilatation of the left auricle, dilatation of the pulmonary vessels and moderate enlargement of the right ventricle and right auricle. Fluoroscopy showed a large mass of calcification in the region of the mitral valve. Our interpretation was "combined valvular heart disease, primarily mitral, with calcification of the mitral valve."

The patient did not respond well to therapeutic attempts and died the day following admission. Autopsy was refused.

COMMENT

Cases 3 and 4 are examples of mitral stenosis in which the diagnosis can be materially aided by x-ray examination. In case 3 the presumptive diagnosis was pulmonary tuberculosis but the correct diagnosis could

have been made by a competent cardiologist. It was easily made by fluoroscopic examination. In case 4 the electrocardiogram gave the first hint as to the correct diagnosis, and again it was easily verified by fluoroscopic examination. It could have been made (and was in case 3) by x-ray examination independent of the history and physical examination. It could have been suspected from her constitutional type, as she was of Irish descent, with red hair, a fair complexion and many freckles. There had been a previously unexplained moderate hypochromic anemia for years, variable in degree, and intermittent menorrhagia, all frequent concomitants of rheumatic heart disease in New England.

SUMMARY AND CONCLUSIONS

Mitral stenosis can be diagnosed in a high percentage of cases by careful roentgen examination, including fluoroscopy.

The demonstration of a calcified mitral valve is unequivocal evidence of mitral stenosis and also indicates its rheumatic etiology.

Dilatation of the left auricle without general cardiac enlargement is highly presumptive evidence of mitral stenosis.

The diagnosis of mitral stenosis can at times be made by roentgen examination even in the absence of characteristic physical signs—here called "subclinical mitral disease."

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PROGNOSIS IN CARCINOMA OF THE RECTUM

A COMPARISON OF THE BRODERS AND DUKES METHODS OF CLASSIFICATION

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In recent years a signal advance has been made in determining the operability of malignant lesions of the rectum and sigmoid, and methods have been evolved by which it is now possible to determine with fair accuracy the probable length of life of individuals following removal of such lesions. Operability can be determined by proctoscopic examination, digital examination of the terminal portion of the colon and bimanual examination of the pelvis. Much of prognostic significance may be learned by such methods, but little can be determined in this manner concerning length of life following radical removal of carcinoma.

A valuable single criterion by which the surgeon can usually decide, before operation, the probable length of life of a patient following radical extirpation of malignant lesions has been provided by one of us,[1] namely the numerical microscopic grading of such tumors. By using such a method the surgeon or pathologist is able to recognize certain cellular changes which are of significance in determining operability, mortality and the probable period of survival following operation. The earliest study was made in 1920 on a series of 537 patients suffering from epithelioma of the lip. It was then that four grades of malignancy were described, but in 1925 this method of grading was altered so that grade 1 included those lesions in which from nearly 100 to 75 per cent of the cells are differentiated, grade 2 from 75 to 50 per cent, grade 3 from 50 to 25 per cent, and grade 4 from 25 to 0 per cent. The grading of carcinoma on a basis of cellular differentiation is a natural application of the general biologic principle that, as a cell becomes differentiated or specialized, its power to reproduce is decreased. One of us[2] said that "a carcinoma whose cells increase in geometric progression without differentiation beyond the point of reproduction would grow faster and be more malignant than one that caused a number of cells to differentiate beyond the point of reproduction."

The high power photomicrographs in figures 1 and 2 show the relative proportion of differentiated and undifferentiated cells in grades 1, 2, 3 and 4.

In grade 1 carcinomas the cells are columnar; the nuclei are not prominent and are smaller than in grade 2. They approach closely the appearance of normal mucous membrane. The low power arrangements of cells in the two grades may closely resemble each other.

In grade 2 the cells are less columnar and the nucleus forms a more prominent part of the cell. The nucleoli are relatively larger, and well formed acini are nearly always present.

In grade 3 the cells are larger and definitely round, and the nucleus takes up nearly all of the cell. Acini may be present but are usually poorly formed. The low power arrangement of cells may closely resemble that of grade 2, but when the majority of cells are large and rounded and the nuclei are nearly as large as the cell, the carcinoma should be graded 3.

In general, the cells in grade 4 lesions tend to be large, hyperchromatic and round and have dedifferentiated so far that they bear little resemblance to the cells of the colonic mucous membrane. Both the low power and the high power views reveal definite characteristics, and there is less chance of error in a consideration of these cells than in the cells of a grade 2 carcinoma. MacCarty[3] has discussed the cytologic aspect of the carcinoma cell, and he stressed the volume relationship between the nucleolus, the nucleus and the whole cell in reparative regenerative cells and in malignant regenerative cells. He found that the nucleolar-nuclear area ratio varies from approximately 1:23 in malignant cells to 1:50 or more in reparative regenerative cells.

In 1926 Lockhart-Mummery[4] adopted a method of classifying carcinoma of the rectum based on clinical and pathologic factors. He arranged his cases in three groups, as follows: class A, small movable lesions which did not appear to involve the muscular coat or the lymph nodes; class B, lesions which appeared to involve the muscular coat but were not fixed and the lymphatic involvement of which was not extensive, and class C, large growths which were fixed and in which there was evidence of extensive lymphatic involvement.

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Abridgment of thesis submitted by Dr. Laird to the Faculty of the Graduate School of the University of Minnesota in partial fulfilment of requirements for the degree of Master of Science in Proctology.

1. Broders, A. C.: Squamous-Cell Epithelioma of the Lip: A Study of Five Hundred and Thirty-Seven Cases, J. A. M. A. **74**: 656-664 (March 6) 1920; Cancer's Selfcontrol, M. J. & Rec. **121**: 133-135 (Feb. 4) 1925.

2. Broders, A. C.: The Grading of Carcinoma, Minnesota Med. **8**: 726-730 (Dec.) 1925.

3. MacCarty, W. C.: Microscopic Grading of Tumors: Its Interpretation, Limitations, and Relation to Radiosensitivity, Am. J. Roentgenol. **37**: 365-367 (March) 1937; A Cytologic Key to the Diagnosis and Prognosis of Neoplasms, J. Lab. & Clin. Med. **13**: 354-365 (Jan.) 1928.

4. Lockhart-Mummery, J. P.: Two Hundred Cases of Cancer of the Rectum Treated by Perineal Excision, Brit. J. Surg. **14**: 110-124 (July) 1926.

Dukes [5] modified this arrangement so that in class A he included lesions which were definitely limited to the wall of the rectum without extrarectal extension or metastasis to lymph nodes. In class B he placed growths which had spread by direct extension to extrarectal tissues but had not invaded the lymph nodes. He considered all carcinomas in which metastasis was present in the regional lymph nodes to be in class C.

In 1933 Wood and Wilkie [6] studied 100 resected specimens of carcinoma of the rectum, classified them according to the Dukes method and divided them histologically into four grades. Their method of histologic gradation was not that of Broders but was modified in that the grading was done on the low power arrangement of cells instead of the degree of differentiation of cells. They believed that the early stage of carcinoma is represented by a flattened plaque in the mucous membrane and that the least malignant tumors tend to grow toward the lumen and take on a papilliferous appearance. High grade tumors with deeply penetrating tendencies remain flat or have only moderately elevated margins. W. W. Mayo [7] expressed the same opinion many years ago. Mucoid carcinomas with signet ring cells were believed to be the most malignant.

TABLE 1.—*Comparison of Five Year Survival Rates According to Class of Lesion (Lockhart-Mummery, Dukes) in Five Different Investigations*

Class of Patients	Gabriel, Dukes and Bussey 1935	Dukes 1936	Gordon-Watson 1938	Lockhart-Mummery 1938	Broders, Buie and Laird 1938
Number of patients surviving and traced	100	142	88	280	354
Percentage of patients alive 5 years after resection:					
Class A.....	83.3	86.6	82.7	66.3	79.2
Class B.....	54.5	56.0	55.2	46.8	39.0
Class C.....	14.3	20.9	13.3	25.4	18.7

In 1935 Gabriel, Dukes and Bussey [8] made a study of thirty perineal and seventy perineo-abdominal excisions and grouped them according to the Dukes method of classification. They stretched the resected specimen on a frame and fixed it in 10 per cent solution of formaldehyde. All lymph nodes were measured, located on a drawing of the resected specimen, cut and examined histologically.

Gordon-Watson [9] in 1938 divided eighty-eight specimens of carcinoma removed by perineal excision into classes according to the method of Dukes [5] and reported the number of years each patient in the series had lived. In 1938 Lockhart-Mummery [10] published the results of his personal experience with 388 patients treated by perineal excision and recorded the grades of growth according to the Dukes method, the immediate operative result and the length of life of each patient. In each of the aforementioned investigations the percentage of five year survivals, based on the patients who survived operation and were traced, was determined for each class, and these are shown in table 1.

5. Dukes, Cuthbert: The Classification of Cancer of the Rectum, J. Path. & Bact. **35**: 323-332 (May) 1932.

6. Wood, W. Q., and Wilkie, D. P. D.: Carcinoma of the Rectum: An Anatomico-Pathological Study, Edinburgh M. J. **40**: 321-343 (July) 1933.

7. Mayo, W. W.: Personal communication to W. J. Mayo and from him to A. C. Broders.

8. Gabriel, W. B.; Dukes, Cuthbert, and Bussey, H. J. R.: Lymphatic Spread in Cancer of the Rectum, Brit. J. Surg. **23**: 395-413 (Oct.) 1935.

9. Gordon-Watson, Charles: Origin and Spread of Cancer of the Rectum, in Relation to Surgical Treatment, Lancet **1**: 239-245 (Jan. 29) 1938.

10. Lockhart-Mummery, J. P.: The Treatment of Cancer of the Rectum, Surg., Gynec. & Obst. **66**: 527-533 (Feb.) 1938.

A study of the work and the conclusions of these investigators prompted the present investigation. It was felt that by taking new specimens from resected growths and studying them according to both the Broders and the Dukes method a comparative study might bring forth interesting inferences and establish substantial conclusions. Accordingly, the records of all patients treated for carcinoma of the rectum and rectosigmoid at the Mayo Clinic during the years 1920, 1921, 1929 and 1930 were collected, and since only those instances in which radical resection of the tumor was performed would serve our purpose, all other records were deleted. Thus 432 records were found to fit all requirements. In addition, 250 cases, making a total

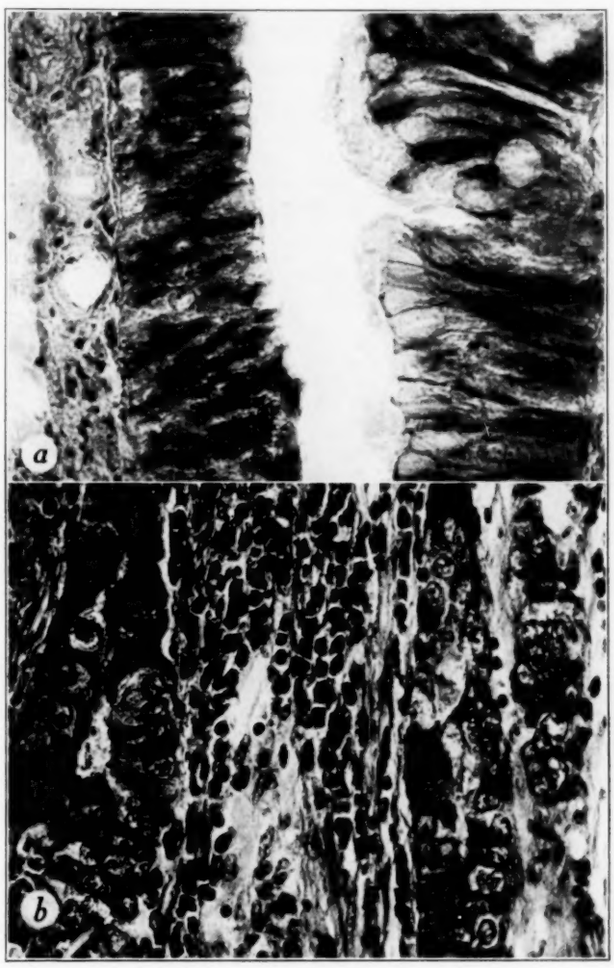

Fig. 1.—Section of a grade 1 carcinoma of the rectum (*a*); the cells are columnar; the nuclei are not prominent and are smaller than those in grade 2 lesions. They approach closely the appearance of normal mucous membrane (hematoxylin and eosin stain; slightly reduced from a photomicrograph with a magnification of 400 diameters). Section of a grade 2 carcinoma of the rectum (*b*); the cells are less columnar and the nuclei form a more prominent part of the cell. The nucleoli are relatively larger and are well formed; acini are often present (hematoxylin and eosin stain; slightly reduced from a photomicrograph with a magnification of 400 diameters).

of 682, in which only colostomy or exploration was performed were included for the study of auxiliary problems. A suitable follow-up procedure was established in order to gather information regarding the length of life of the patient following the operation.

Second, all pathologic specimens removed at operation were reexamined. A longitudinal incision was made, exposing the mucosal surface of the bowel, so that the conformation of the lesion would be disturbed as little as possible. A sketch was made to actual size of the plane surface of the lesion and the portion of ulcera-

tion. The position of the lesion was established by measuring and recording its distance above the external anal margin. Approximately every three sixteenths of an inch (5 mm.) for the full length of the specimen, incisions were carried transversely to the long axis of the bowel from the serosal to the mucosal surface. By this means the thin slices hinged on the uncut mucous membrane, facilitating examination of lymph nodes (fig. 3). A sketch of a section of the specimen was made to show the depth of ulceration and the degree of penetration of the wall of the bowel by the carcinoma. Lymph nodes were frozen, sectioned and stained with Terry's neutral polychrome methylene blue. Those nodes that were seen to be free from metastasis were represented in the sketch by clear circles, and those that were involved were indicated by filled in circles. If one lymph node was found to contain metastasis, no further nodes were examined microscopically. One or more blocks of tissue were taken at the points of deepest penetration of the carcinoma, and their relative positions were indicated on the sketches. Photographs of the gross specimens in classes A, B and C are shown in figures 4 and 5. The Dukes classification of the growth was recorded. In a few instances, classification was deferred until the block could be examined microscopically. Usually the first impression as to the degree of extension was unchanged by microscopic examination. One growth thought to be class B on gross inspection was changed to class A after microscopic examination (fig. 6). The blocks of tissue, identified by the patient's number, were frozen, sectioned and stained with hematoxylin and eosin. Some blocks of tissue from specimens obtained in 1920 and 1921 were immersed in a 3 per cent solution of ammonium hydroxide for twelve hours and were then replaced in 10 per cent solution of formaldehyde in order to improve staining qualities.

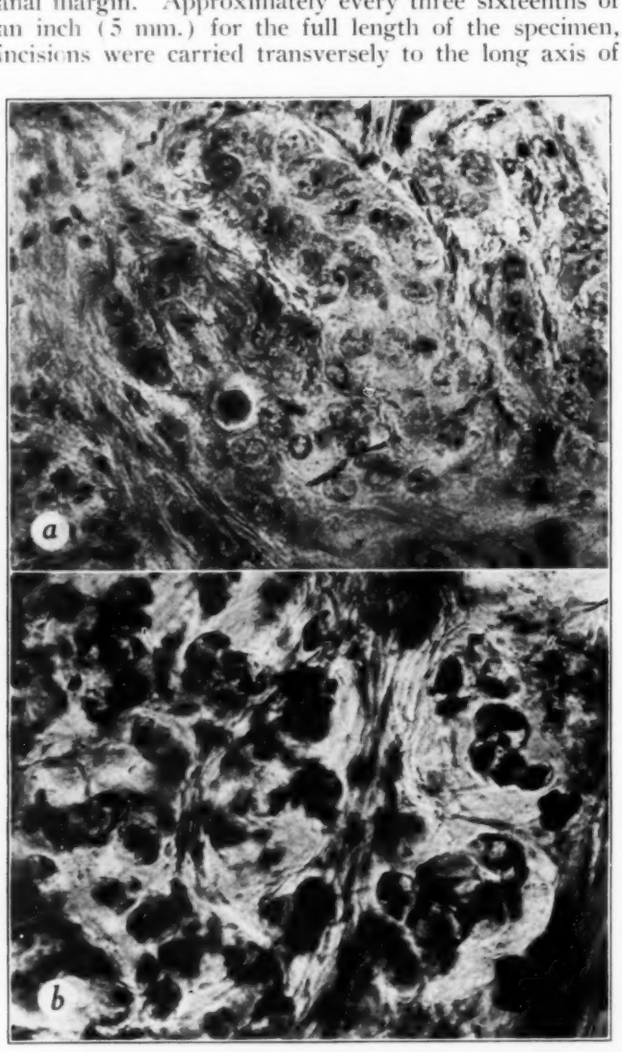

Fig. 2.—Section of a grade 3 carcinoma of the rectum (*a*); the cells are larger and definitely round, and the nucleus occupies nearly all of the cell; acini, when present, are usually poorly formed (hematoxylin and eosin stain; slightly reduced from a photomicrograph with a magnification of 400 diameters). Section of a grade 4 carcinoma of the rectum *b*; the cells are usually large, hyperchromatic and round; they bear little resemblance to the cells of the mucous membrane of the colon (hematoxylin and eosin stain; slightly reduced from a photomicrograph with a magnification of 400 diameters).

TABLE 2.—*Distribution According to Histologic Grade of Malignancy (Broders) in 682 Cases, Comprising the Total Series Examined*

Type of Surgical Treatment	Total Patients	Grade of Malignancy 1 Patients	1 Per Cent	2 Patients	2 Per Cent	3 Patients	3 Per Cent	4 Patients	4 Per Cent
Colostomy or exploration only.....	250	50	20.0	129	51.6	50	20.0	21	8.4
Some form of resection.....	432	73	16.9	241	55.8	100	23.1	18	4.2
Total.....	682	123	18.0	370	54.2	150	22.0	39	5.7

Third, the sections were studied microscopically by the method of Broders and the grade was recorded on each slide. According to the Dukes method, the drawings were examined, verified histologically and recorded on the slide. This information, with the sketch, was then added to a card on which the other pertinent data had been previously recorded. In this way the grading was established without knowledge of any other facts in the case.

In a few instances, involvement of lymph nodes found on the first examination was not found on reexamination. When this occurred the original report was accepted.

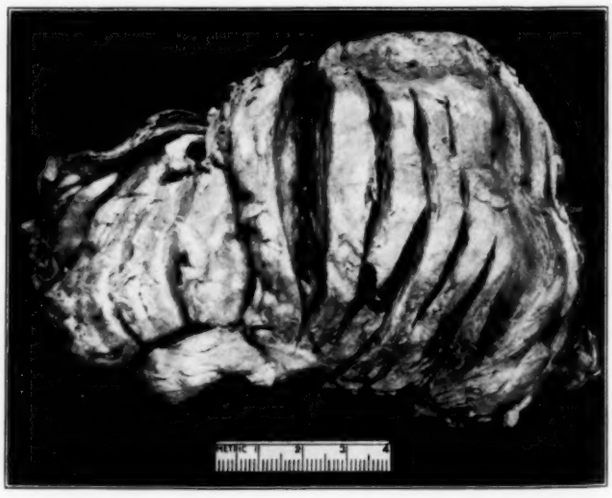

Fig. 3.—Illustrating the manner in which specimens in this series were cut for examination of lymph nodes.

DISTRIBUTION BY GRADE

Table 2 shows the distribution according to Broders' gradation in 682 cases in which surgical treatment had been administered. Table 3 compares the grading by different authors in resected growths. Close agreement is apparent and indicates that, if the Broders method is followed carefully, results should be consistent. The reason for the difference between the series of Broders

and the present series may be understood by comparing the distribution of grade 4 in 1920 and 1921 with grade 4 in 1929 and 1930. It should be remembered also that this is a comparison of grades of resected specimens and not of distribution in general. In 1920

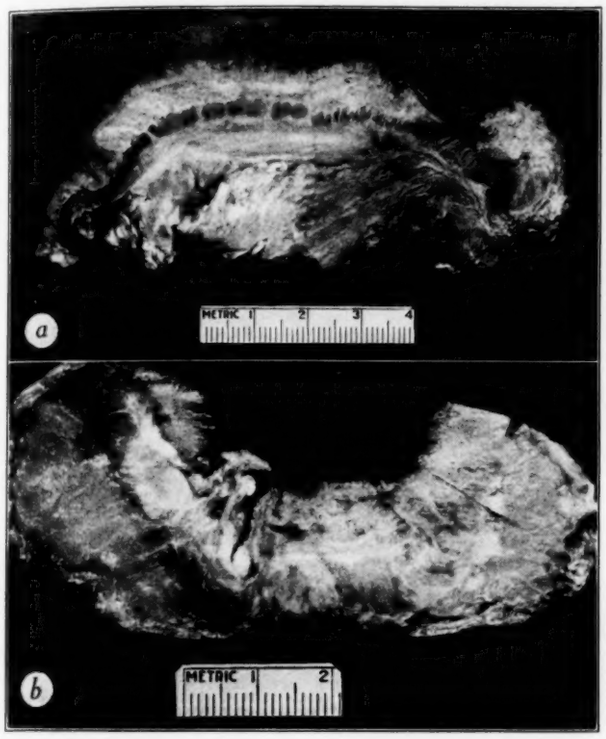

Fig. 4.—Carcinoma of the rectum (*a*), class A, grade 4; the carcinoma apparently did not penetrate the musculature of the rectum at any point; carcinoma of the rectum (*b*), class B, grade 2; the carcinoma has penetrated the musculature in several places.

and 1921 grade 4 represented 7.2 per cent of 152 resected specimens, and in 1929 and 1930 only 2.5 per cent of 280 specimens were classified in this group. This difference was the result of the fact that in 1929

TABLE 3.—*Percental Distribution of Grades of Malignancy—2,210 Resected Neoplasms Reported in Four Investigations*

Series	Total Cases Reported	Percentage in Grade of Malignancy 1	2	3	4	Colloid
Broders, Bule and Laird	432	16.9	55.8	23.1	4.2	
Rankin and Broders.....	598	17.6	50.0	23.5	8.9	
Broders.....	580	14.6	51.8	24.5	9.1	
Dukes.....	600	6.0	54.0	26.0	2.0	12.0

and 1930 some surgeons did not favor the surgical removal of grade 4 lesions because of the unfavorable outlook for the patient. The discrepancy between the percental distribution in the Dukes series and ours can be explained by two factors. First, Dukes [11] failed to follow accurately the Broders [12] method of grading. In his article "Histological Grading of Rectal Cancer" he said:

> The system of grading tumors described by Broders supplies such a standard. . . . It can be applied easily to malignant growths of the adenocarcinoma type provided one bases the judgment on a general survey and not on a single field of the microscope. Actually the decision as to the grade of malignancy is more dependent on the arrangement of the cells than on the relative number of so-called undifferentiated cells.

11. Dukes, Cuthbert: Histologic Grading of Rectal Cancer, Proc. Roy. Soc. Med. **30:** 371-376 (Feb.) 1937.
12. Footnotes 1 and 2.

This accounts for the comparatively low percentage of the grade 1 growths. Many grade 1 lesions have the general histologic arrangement of the average grade 2 growths, and it is only by considering the relative number of dedifferentiated cells and their degree of dedifferentiation that the proper distinction can be made. The second factor is that Dukes [11] graded colloid carcinoma separately. We do not believe that this is necessary.

There is difference of opinion as to the degree of malignancy of colloid carcinoma. Some observers believe that formation of mucus is a sign of functional

TABLE 4.—*Operative Mortality and Three and Five Year Survival Rates According to Class of Lesion (Lockhart-Mummery and Dukes)—426 Traced Patients Out of 432 Operated On*

Class	Patients Operated On	Patients Traced	Operative Mortality,* per Cent	Percentage of Patients Alive After 3 Years	Percentage of Patients Alive After 5 Years
A	116	115	12	76.5	69.6
B	121	120	16	51.6	32.2
C	195	191	20	31.5	14.6

* All patients who died within a month in the hospital are included in the operative mortality.

differentiation of the carcinoma cell and that carcinomas showing mucoid degeneration possess a relatively low degree of malignancy. Others believe that mucoid carcinomas, which are the most undifferentiated structurally, secrete the most mucinous material. Raiford [13] stressed the importance of distinguishing between true primary mucoid carcinoma and mucoid degeneration. He preferred the term "mucoid carcinoma" to "colloid

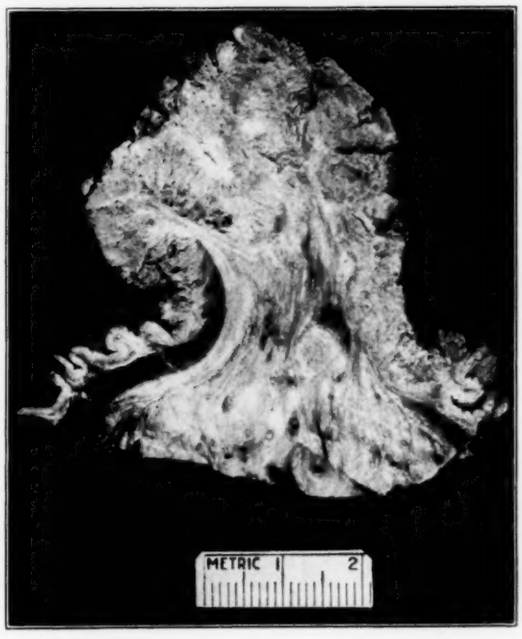

Fig. 5.—Carcinoma of the rectum, class C, grade 1.

carcinoma," and in a series of 166 rectal carcinomas he found five primary mucoid carcinomas and thirty-six which showed mucoid degeneration. In our series we found only eight mucoid carcinomas, and all were graded either 3 or 4. We found mucoid degeneration frequently in the lower grade lesions. Raiford's [13] table shows the results of treatment of forty-one patients;

13. Raiford, T. S.: Mucoid Carcinoma of the Gastro-Intestinal Tract: So-Called Colloid Cancer, Surg., Gynec. & Obst. **55:** 409-417 (Oct.) 1932.

18 per cent (of eleven patients who had primary mucoid carcinomas) were alive at the end of five years, and 56 per cent of those who had adenocarcinomas and mucoid degeneration were living five years after treatment. He stated that the degree of the formation of mucus is inversely proportional to the grade of malig-

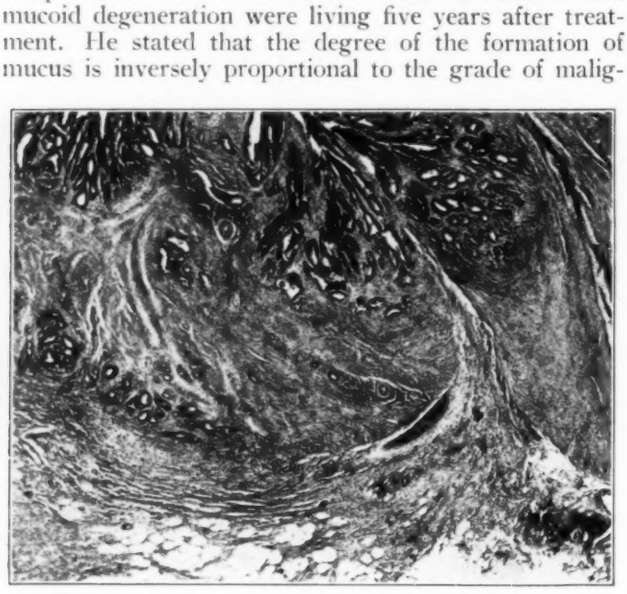

Fig. 6.—Section of a carcinoma which has extended just to the fascia propria of the rectum (hematoxylin and eosin stain; slightly reduced from a photomicrograph with a magnification of 15 diameters).

nancy. This view is supported by Ochsenhirt,[14] who studied 188 carcinomas in which the secretion of mucus was prominent. Rankin and Olson [15] found forty-four cases of colloid carcinoma in a series of 453 cases of carcinoma of the colon. They believed that the prognostic difference between colloid and other carcinomas is not great but that colloid carcinomas are likely to present a more serious problem. They did not divide their cases into those involving mucoid carcinomas and those involving carcinomas with mucoid degeneration.

DISTRIBUTION ACCORDING TO CLASS

In this series of 432 resected specimens, 116, or 26.85 per cent, were classed as A, 121, or 28 per cent, as B, and 195, or 45.15 per cent, as C (table 4). Dukes,[11]

TABLE 5.—*Percental Distribution According to Class of Malignancy (Lockhart-Mummery and Dukes)—Comparison of the Results in Five Investigations*

Series	Total Patients	Per Cent		
		Class A	Class B	Class C
Broders, Bule and Laird	354	28.5	28.2	43.2
Dukes	142	21.0	35.2	43.6
Lockhart-Mummery	354	30.0	42.3	27.7
Wood and Wilkie	59	22.0	42.3	35.6
Gabriel, Dukes and Bussey	87	27.6	40.2	32.2

reporting a long series of cases of carcinoma of the rectum in which the lesions had been accepted by surgeons as being operable, gave the distribution as follows: class A, 15 per cent; class B, 35 per cent, and class C, 50 per cent. However, in a series of 142 patients who survived operation, the percental distribution approximates that in this series. This is shown in table 5, which includes the record of other investigators who have used the Dukes classification. In this table is also shown the percental distribution among 354 cases of our series which were selected so as to be comparable with the other series in this table.

The percental distribution according to class is a measure of the type of lesion that the surgeon usually removes at operation, and the lesion is therefore one that is considered operable. It is evident in Lockhart-Mummery's [4] series that he has recently accepted a greater proportion of class C lesions as operable.

TABLE 6.—*Operative Mortality and Three Year and Five Year Survival Rates According to Grade of Malignancy (Broders)—426 Traced Patients Out of 432 Operated On*

Grade	Patients Operated On	Patients Traced	Operative Mortality,* per Cent	Percentage of Patients Alive After 3 Years	Percentage of Patients Alive After 5 Years
1	73	73	7.0	85.0	65.7
2	241	237	16.6	48.9	31.6
3	100	98	22.2	35.7	22.4
4	18	18	28.0	16.6	11.1

* All patients who died within a month in the hospital are included in the operative mortality.

When the distribution of "class" and "grade" are compared (fig. 7), it is found that in grade 1 lesions the proportion of class A to class C growths is approximately 3:1; in grade 2, 1:2; in grade 3, 1:5; and in grade 4 the proportion would be greater than 1:10 if those cases in which metastasis is present were included. Because only those grade 4 lesions in which prognosis was extremely favorable for the patients were operated on in 1929 and 1930, the proportion of class A to class C lesions was smaller.

We compared the percentages of five year survivals of patients whose lesions were in classes A, B and C as reported in four other investigations and ours (table 1). Our calculations in this instance were based on the 354 cases which were comparable to those in the other series. The percentages of five year survivals of patients in each class do not coincide exactly, but the figures are in close enough agreement for their differ-

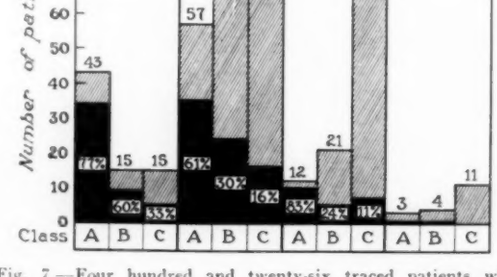

Fig. 7.—Four hundred and twenty-six traced patients whose lesions have been graded and classed, showing the relationship of distribution, grade, class and five year results. The numbers in the black columns indicate patients (per cent) alive at the end of five years for each class and grade of lesion, calculated from the number of traced patients with each class and grade of lesion who underwent resection. The height of the shaded columns indicates the number of patients who underwent some form of surgical excision and who have been traced.

ence to be explained by the variation in the type of operation done.

Operative mortality is four times as great among patients who have grade 4 lesions as among those who have grade 1 tumors (table 6), and the chance of surviving five years after operation for a patient who has

14. Ochsenhirt, N. C.: The Significance of Mucus-Forming Cells in Carcinoma of the Large Intestine and Rectum, Surg., Gynec. & Obst. **47**: 32-35 (July) 1928.

15. Rankin, F. W., and Olson, P. F.: The Hopeful Prognosis in Cases of Carcinoma of the Colon, Surg., Gynec. & Obst. **56**: 366-374 (Feb.) 1933.

a grade 4 lesion is 11 per cent, about a sixth of that for patients who have grade 1 lesions. These facts lend justification to the conservatism of those surgeons who observe caution and often refuse to operate on patients who have grade 4 carcinomas.

The operative mortality of patients who have class C lesions is almost twice that of patients whose lesions are in class A, whereas the chance of surviving five years for a patient who has a class C lesion is a fifth as great as in one who has a class A lesion (table 4). If the percentage of five year survival of patients is calculated, the rate for those who have class A lesions is 69.6 per cent, for those who have class B lesions 32.2 per cent and for those who have class C lesions 14.6 per cent. On the same basis, the five year survival rate for patients who have grade 1 lesions is 65.7 per cent, for those who have grade 2 lesions 31.6 per cent, for those who have grade 3 lesions 22.4 per cent, and for those who have grade 4 lesions 11.1 per cent (table 6).

The relationship of grading and class to the five year survival rate has been discussed. Figure 7 shows the distribution and the relationship of grade and class to the five year survival rate. In this figure an actual and relative decrease in the number of patients who are alive five years after operation is shown as the grade increased from 1 to 4 and as the growth advanced from A to C in each grade. The advantage of combining the two classifications in relationship to the number of patients alive five years after resection is clear. In each grade the ratios of five year cures are approximately three, two and one with respect to class A, B and C. For example, 65.7 per cent of all patients who have a grade 1 carcinoma and who survive operation are alive five years after resection (table 6). In grade 1 cancers the chance that the resected specimen is in class A is three times that of its being in class C. According to whether the growth removed is in class A, B or C of grade 1, the chances for survival of the patient five years after operation are, respectively, 77 per cent, 60 per cent and 33 per cent (fig. 7).

On the basis of our studies, it can be said that 22.4 per cent of all patients who survive resection of a grade 3 carcinoma will be alive five years after operation (table 6). There is a 65 per cent chance that a grade 3 tumor will be in class C, in which patients who have such a lesion have a five year survival rate of 11 per cent. There is a 21 per cent chance that the lesion will be in class B, in which patients having such a lesion have a 24 per cent chance of a five year cure, and there is a 12 per cent chance that the lesion will be in class A, in which patients have an 83 per cent chance of living five years or longer (fig. 7).

As the grade increases from 1 to 4 there is a proportionately lessened chance that the patient will be alive five years after operation, and patients who have class A lesions in each grade except grade 4 have a better chance of being alive five years after operation.

We wished to determine whether or not carcinomas of high grade grew faster and caused death more quickly than those of lower grades. The average duration of life was therefore calculated for patients, according to lesions in each grade, who had survived operation for less than five years. The average duration of life of such patients who had grade 1 carcinomas was 29.5 months; grade 2, 26.5 months; grade 3, 25 months, and grade 4, 20 months. On the basis of such evidence it would appear that the rate of growth or at least the speed with which metastases terminate life is directly proportionate to the grade of malignancy.

SUMMARY AND CONCLUSIONS

Four hundred and thirty-two resected specimens of carcinoma of the rectum were graded according to the Broders [12] method and also grouped according to the Dukes method of classification. The distributions of grade and class were studied in comparison with other investigations and also in relationship to survival after operation. On the basis of the entire study, certain conclusions were reached:

1. The presence or absence of mucus loses importance as a guide to prognosis if histologic grading is done by the Broders method.

2. Tumors of higher grades are more rapid in growth and their metastases cause the death of the patient earlier than those of lower grades.

3. The classification of the lesion according to the method of Dukes is also correlated with postoperative life; the higher the class, the less the percental survival.

4. A combination of the Broders grading and the Dukes classification yields a prognosis of survival more accurate than either method taken separately.

EXPERIMENTAL WESTERN EQUINE ENCEPHALOMYELITIS

SUCCESSFUL TREATMENT WITH HYPERIMMUNE RABBIT SERUM

JOSEPH ZICHIS, PH.D.
AND
HOWARD J. SHAUGHNESSY, PH.D.
CHICAGO

There is a general impression that treatment of a disease in which the etiologic agent is a virus is of no value after the infection has become established. Rivers [1] probably presented the opinion of other authorities as well as his own when he wrote the following in 1936: "Such a phenomenon throws light on the clinical observations that the administration of convalescent or immune serum to an individual in whom the signs and symptoms of a virus disease are already manifest is without value." It is of interest that Rivers [2] has indicated (in the Lane lectures given by him in 1939) that he has modified his point of view to the extent of admitting that measles can be treated after the onset of the typical early signs and symptoms of the disease. However, the majority of clinicians and investigators hold to the view expressed by this authority in 1936. The conception that "once a virus has entered a cell no amount of antiserum brought in contact with the cell can injure the virus or hinder its activity" has resulted from the investigations of several groups of competent workers [3] on serum therapy of virus infections of tissue cultures. If this is admitted as a fact,

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1. Rivers, T. M.: Recent Advances in the Study of Viruses and Viral Diseases, J. A. M. A. **107:** 206-210 (July 18) 1936.

2. Rivers, T. M.: Lane Medical Lectures: Viruses and Virus Diseases, Stanford Univ. Publ., Univ. Series M. Sc. **4:** 1-33, 1939.

3. Rivers, T. M.; Haagen, E., and Muckenfuss, R. S.: Observations Concerning Persistence of Living Cells in Maitland's Medium for Cultivation of Vaccine Virus, J. Exper. Med. **50:** 665-672 (Nov.) 1929. Andrewes, C. H.: Virus III in Tissue Cultures: Further Observations on Formation of Inclusion Bodies; Experiments Bearing on Immunity, Brit. J. Exper. Path. **10:** 273-280 (Aug.) 1929; Antivaccinal Serum: Evidence of Slow Union with Virus in Vitro, J. Path. & Bact. **33:** 265-272 (April) 1930. Downie, A. W., and McGaughey, C. A.: Experiments with Virus of Ectromelia: Action of Immune Serum in Vivo and on Growth of Virus in Culture, ibid. **40:** 297-310 (March) 1935. Sabin, A. B.: Mechanism of Immunity to Filtrable Viruses; Fate of Virus in System Consisting of Susceptible Tissue, Immune Serum and Virus, and Role of Tissue in Mechanism of Immunity, Brit. J. Exper. Path. **16:** 84-101 (Feb.) 1935.

it seems equally apparent that all cells are not invaded at once in most virus infections at least. From studies of infections in tissue cultures it has also been learned that, if serum is brought into contact with cells before their exposure to virus, infection may be aborted. Therefore, even after the development of early signs and symptoms of a disease, the administration of serum should be of value to the person or animal by penetrating the cells surrounding the parasitized cell and neutralizing any virus which attempts to invade them. The acceptance of these premises suggests that investigation of the effect of serum on the whole organism infected by a disease should give one a better understanding of the potentialities of serum therapy than do studies made on infected cells in tissue cultures.

killed more than one month later. This is compared with the control group in which only one of the five recovered animals showed extensive pulmonary lesions. Practically all the remaining animals in both groups of serum treated mice showed some pulmonary lesions while three of the five survivors in the control group had no lesions at all. Laidlaw and his colleagues made this significant statement: "Here it may be noted that these lesions were convincing evidence that the virus had reached and produced damage in the lungs, and that concentrated serum was powerful enough to arrest the pathological process."

Prevention or modification of measles by convalescent or "normal" serum is so generally accepted that it has become a routine service of physicians in many com-

TABLE 1.—*Observations in Experiment 3*

	Treated with Serum at Onset of Fever								Treated with Serum When Animals Were Visibly Ill								Untreated Controls							
	Guinea Pig 1		Guinea Pig 2		Guinea Pig 3		Guinea Pig 4		Guinea Pig 5		Guinea Pig 6		Guinea Pig 7		Guinea Pig 8		Guinea Pig 9		Guinea Pig 10		Guinea Pig 11		Guinea Pig 12	
Days	Temperature*	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms
1	101.2	N	100.0	N	100.0	N	101.3	N	100.0	N	99.6	N	101.4	N	102.0	N	100.2	N	100.0	N	99.8	N	100.0	N
2	100.1	N	101.4	N	99.8	N	101.0	N	101.0	N	100.0	N	100.2	N	101.7	N	100.3	N	100.3	N	100.4	N	102.3	N
3	101.2	..	.....	..	101.0	..	102.3	..																
	102.4	P	100.0	N	100.4	N	101.3	N	102.0	N	100.8	N	100.0	N	100.8	N	100.0	N	102.4	P	101.5	N	102.4	N
4	102.0	..	100.1	..	101.2	..	101.0	..																
	102.3	P	102.0	N	101.4	P	102.8	N†	100.0	N	101.0	N	99.8	N	100.4	N	101.2	N	103.4	P	101.4	N	101.4	N
5	102.0	..	102.0	..	101.8	..	103.8	..																
	103.6	P†	101.6	N	102.4	S†	.....	N	102.8	S†	103.0	N	102.6	P	101.9	P	103.4	S	103.8	S	100.3	P	100.3	N
6	.....	..	101.7																					
		P	104.0	S†	.....	S	.....	N	104.0	S	101.0	P	104.0	S	103.4	P	101.0	Pa	104.0	S	100.0	S	103.8	P
7	.....	N	.....	S	.....	P	.....	N	.....	S	101.4	P	102.8	S†	103.2	S	102.8	Pa	101.0	S	102.4	S	104.0	S
8	.....	N	.....	P	.....	P	.....	N	.....	S†	102.4	Pa†	.....	S	101.0	PR†	98.0	PaM	102.0	S	100.0	S	105.2	S
9	.....	N	.....	P	.....	P	.....	N	.....	P	Dead	..	.....	PR†	.....	S†	Dead	..	102.8	PaM	Dead	..	103.0	S
10	.....	N	.....	N	.....	N	.....	N	.....	P	.....	..	.....	PR	.....	S	.....	..	100.0	PaM	.....	..	100.0	S
11	.....	N	.....	N	.....	N	.....	N	.....	P	.....	..	.....	S	.....	S†	.....	..	Dead	..	.....	..	101.0	S
12	.....	N	.....	N	.....	N	.....	N	.....	N	.....	..	.....	S	.....	S	.....	..	.....	..	.....	..	98.6	Pa
13	.....	N	.....	N	.....	N	.....	N	.....	N	.....	..	.....	S†	.....	S	.....	..	.....	..	.....	..	99.6	Pa
14	.....	N	.....	N	.....	N	.....	N	.....	N	.....	..	.....	S	.....	S	.....	..	.....	..	.....	..	96.4	Pa
15	.....	N	.....	N	.....	N	.....	N	.....	N	.....	..	.....	P	.....	S†	.....	..	.....	..	.....	..	Dead	..
16	.....	N	.....	N	.....	N	.....	N	.....	N	.....	..	.....	P	.....	S	.....	..	.....	..	.....	..	.....	..
17	.....	N	.....	N	.....	N	.....	N	.....	N	.....	..	.....	N	.....	N	.....	..	.....	..	.....	..	.....	..
18	.....	N	.....	N	.....	N	.....	N	.....	N	.....	..	.....	N	.....	N	.....	..	.....	..	.....	..	.....	..
19	.....	N	.....	N	.....	N	.....	N	.....	N	.....	..	.....	N	.....	N	.....	..	.....	..	.....	..	.....	..
20	.....	R	.....	R	.....	R	.....	R	.....	R	.....	..	.....	R	.....	R	.....	..	.....	..	.....	..	.....	..

*, upper temperature a. m., lower p. m.
†, 10 cc. of serum given intraperitoneally.
N, no symptoms.
P, roughened coat, passive, not eating.
S, visibly sick.
Pa, paralyzed.
R, released.
PR, partial paralysis.
M, moribund.

There are several examples of apparently successful serum therapy of virus diseases in man or experimental animals which deserve to be better known. The first of these was the study of serum therapy of influenza in mice reported in 1935 by Laidlaw, Smith, Andrewes and Dunkin.[4] They found that concentrated serum obtained from a hyperimmunized horse had "a beneficial action on mice already infected with virus." In their main experiment the fatality in three groups of twenty-five mice each was as follows: controls given no serum, twenty deaths; mice receiving serum twenty-four hours after injection of virus, eight deaths, and mice receiving serum forty-eight hours after injection of virus, ten deaths. Probably their most striking observations were that ten of the seventeen successfully treated mice that received serum twenty-four hours after infection and ten of the fifteen successfully treated mice that received serum forty-eight hours after infection showed extensive lesions of the lungs when

munities. The general opinion has been, however, that serum therapy is of no value after the catarrhal symptoms have appeared. Until very recent years the few studies which had been made were unsuccessful or inconclusive. Most of the patients treated after onset of clinical symptoms received only from 5 to 10 cc. of convalescent serum by the intramuscular or subcutaneous routes, which is about the prophylactic dose. In 1936 Levinson [5] and in 1939 Levinson and Conner [6] made an attempt to secure objective evidence of the effect of serum therapy of measles after the appearance of clinical symptoms and Koplik spots but before the eruption. They limited their cases to those in the preeruptive stage because of the well known fact that the temperature subsides and symptoms diminish after the appearance of the rash. Their results in the treatment of sixteen patients with measles, fifteen of whom were

4. Laidlaw, P. P.; Smith, Wilson; Andrewes, C. H., and Dunkin, G. W.: Influenza: The Preparation of Immune Serum in Horses, Brit. J. Exper. Path. **16:** 275-291 (June) 1935.

5. Levinson, S. O.: Human Convalescent Measles Serum: Its Use in Prophylaxis and Therapy, Proc. Chicago Inst. Med., vol. **11,** No. 6, June 15, 1936.

6. Levinson, S. O., and Conner, J. A.: The Treatment of Active Measles with Human Convalescent Serum, J. Pediat. **14:** 268 (Feb.) 1939.

hospitalized for other infectious diseases, were striking. Six patients had a normal temperature on the evening of the day the rash appeared, although it is usually stated that the temperature should be highest at about that time. In most of the other cases there was a sharp drop in temperature. The character of the eruption was greatly modified and the alleviation of the other

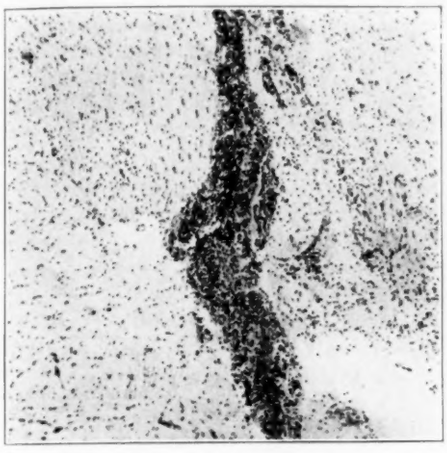

Fig. 1.—Section of brain of untreated guinea pig; × 48.

signs and symptoms, particularly the cough, was marked. In analyzing the reasons for their success and the failure of previous workers it must be emphasized that Levinson and Conner used from 20 to 50 cc. of convalescent serum and administered it intravenously. These dosages are equivalent to from five to ten times those used by other investigators, and the intravenous route made the serum more available. Kohn, Klein and Schwarz [7] also reported that from 40 to 50 cc. of convalescent serum given intravenously in the pre-eruptive or early eruptive stages was successful in modifying the disease. They also found that 200 cc. of "normal" human serum was needed to obtain the same results secured with from 40 to 50 cc. of convalescent serum.

Meyer and Eddie [8] recently reviewed the literature on the treatment of psittacosis by convalescent serum and found that the opinion of most of those who had used it was favorable. They cited a case of their own in which convalescent serum was successfully employed in large dosage and state "The causal relationship between the injection of the serum and the crisis is too apparent to be merely a coincidence." They also observed that convalescent serum is of low potency and that better results should be expected from a hyperimmune serum. While these observations are, of course, not conclusive, they add an impression that another virus disease can be treated successfully with serum if large enough dosages are employed.

While the possibility that man can be infected by the virus of equine encephalomyelitis was pointed out by Meyer [9] a number of years ago, interest in the human disease was first aroused by the Massachusetts epidemic [10] in 1938. Since that outbreak, which is believed to have caused about thirty deaths, a number of other cases have been reported. It is quite natural that serum therapy should have been attempted in the treatment of such a highly fatal disease. However, the isolated reports on the few human cases of equine encephalomyelitis treated with serum have been either disappointing or unconvincing. These results are probably not significant in view of the relatively small dosage of serum employed and the lack of knowledge concerning its potency.

The only previous report that we have seen on the use of serum in the treatment of equine encephalomyelitis in experimental animals is that of Wyckoff and Tesar.[11] These investigators worked with a commercial unrefined hyperimmune horse serum. Unfortunately no data were presented concerning its potency. Monkeys each receiving 10 cc. of this serum twenty-four and three hours respectively before intranasal instillation of virus were protected. They were not immune when tested by another intranasal instillation of virus seven weeks later, indicating that their immunity had been due to "passive inhibition of infection." Monkeys given 10 cc. of serum at the first appearance of fever and again twenty-four hours later were not benefited in any way. This was true with the use of both Western and Eastern serums. In another series of experiments Wyckoff and Tesar gave 10 cc. of serum intravenously to monkeys three or twenty-four hours after virus was administered intranasally. Three of the six monkeys treated in this manner were protected but were reinfected intranasally seven weeks later, indicating that the protection "had been essentially passive." They concluded that serum "given at the time of first symptoms (fever), or later, has been without beneficial influence upon the course of either Eastern or Western disease."

This is a progress report of our studies on the treatment of Western equine encephalomyelitis with rabbit

Fig. 2 (guinea pig 8, table 2).—Section of brain of guinea pig treated with serum when visibly ill; killed twelve days after treatment; × 48.

hyperimmune serums. It should be emphasized that the potency of rabbit serum prepared in this laboratory was much higher than that of commercial horse serums which we have tested. The protection test used in standardizing our serum is also a more rigorous procedure than the in vitro neutralization test commonly employed.

7. Kohn, J. L.; Klein, I. F., and Schwarz, Herman: Treatment of Preeruptive Measles with Convalescent Serum, J. A. M. A. **111:** 2361-2364 (Dec. 24) 1938.

8. Meyer, K. F., and Eddie, B.: The Value of the Complement Fixation Test in the Diagnosis of Psittacosis, J. Infect. Dis. **65:** 225 (Nov.-Dec.) 1939.

9. Meyer, K. F.: A Summary of Recent Studies on Equine Encephalomyelitis, Ann. Int. Med. **6:** 645 (Nov.) 1932.

10. Fothergill, L. D.; Dingle, J. H.; Farber, Sidney, and Connerlev, M. L.: Human Encephalomyelitis Caused by the Virus of the Eastern Variety of Equine Encephalomyelitis, New England J. Med. **219:** 411 (Sept. 22) 1938. Feemster, R. F.: Outbreak of Encephalitis in Man Due to the Eastern Virus of Equine Encephalomyelitis, Am. J. Pub. Health **28:** 1403 (Dec.) 1938.

11. Wyckoff, R. W. G., and Tesar, W. C.: Equine Encephalomyelitis in Monkeys, J. Immunol. **37:** 329 (Oct.) 1939.

METHODS AND MATERIALS

Virus.—The Western equine encephalomyelitis virus was employed in these studies. The strain used was obtained from Dr. Carl Ten Broeck of the Rockefeller Institute for Medical Research in January 1939 and was labeled "Western E. E. Kelser." In this laboratory the virus has been maintained by serial intracerebral passages in guinea pigs. Since receiving this virus its identity has been established several times by protection tests with a specific immune serum [12] and by cross protection tests with a known Western equine encephalomyelitis virus.[13]

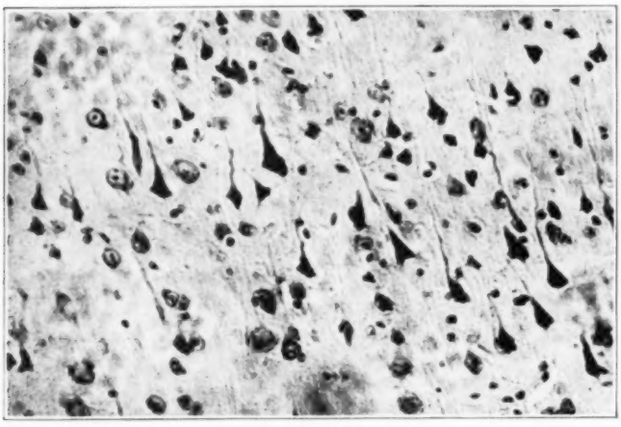

Fig. 3 (guinea pig 5, table 2).—Section of brain of guinea pig treated with serum when visibly ill; killed twelve days after treatment; slightly reduced from a photomicrograph with a magnification of 200 diameters.

In the treatment experiments guinea pig brain virus was used for the inoculation of all the animals, whereas in the hyperimmunization experiments for the production of immune serum a virus which had been cultivated on the developing chick embryo was used. The dilutions of the guinea pig brain virus were made in heart infusion broth in each case, while the chick embryo virus was diluted with buffered physiologic solution of sodium chloride.

Animals.—Guinea pigs of about 400 Gm. and Swiss mice of about 20 Gm. weight were used in the serum treatment studies. Rabbits, each weighing about 4 Kg., were selected for the production of the hyperimmune serum. Rabbits were selected because it is believed that protective antibodies produced in them are of small molecular dimensions and for this reason are probably able to penetrate to the infected tissues more rapidly.

Production of Hyperimmune Serum.—The virus used for the hyperimmunization of the rabbits was propagated on developing chick embryos. After eleven days of incubation the embryos were inoculated through an opening in the shell with a bacteria free virus. Following inoculation on the chorio-allantoic membrane the eggs were sealed with paraffin and reincubated until the embryo died. As a rule all the embryos were dead within twenty hours after inoculation. The embryos were then removed from the eggs and ground in a tissue mill. The minced tissue was adjusted to a 20 per cent suspension with buffered physiologic solution of sodium chloride, following which the suspension was centrifuged for fifteen minutes at 2,000 revolutions per minute to remove tissue particles. The preparation of this virus was carried out under strict aseptic precautions and only virus that was found to be free of bacterial contamination was used for hyperimmunization of the rabbits. The minimum lethal dose of the virus was about 10^{-10} for Swiss mice.

Each rabbit was injected subcutaneously with two 3 cc. doses of Western virus chick embryo vaccine treated with formaldehyde. The injections were made seven days apart, and ten days after the last dose each rabbit was injected intravenously with 0.5 cc. of the 20 per cent living virus suspension. Thereafter the animals were injected intravenously on Monday, Wednesday and Friday of each week, the dose being doubled at each injection until the maximum amount of 5 cc. was reached. It was found necessary to follow this schedule of immunization for at least twelve weeks before a serum of high potency could be obtained.

Determination of Potency of Serum.—The protective value of the serum was determined on Swiss mice. The test consisted of injecting each of six mice subcutaneously with 1 cc. of one of the following dilutions of the serum: (1) undiluted, (2) 1:100, (3) 1:500, (4) 1:1,000 and (5) 1:1,200. Twenty-four hours after the inoculation of the serum each mouse was injected intracerebrally with 0.03 cc. of a 1:10,000 dilution (about ten times the minimum lethal dose) of guinea pig brain virus. To demonstrate the virulence of the virus, six normal mice were similarly injected with the same preparation of the virus. The mice were kept in individual cages and were observed for twenty-four days.

In these experiments a lot of rabbit hyperimmune serum was not used unless 1 cc. of a 1:1,000 dilution protected at least two thirds of the mice in the potency test. The serum was not concentrated and did not contain a preservative. Rabbit serum was employed in all experiments excepting experiment 4, in which a commercial horse serum was used.

EXPERIMENTS

EXPERIMENT 1.—Each of fourteen Swiss mice was inoculated intracerebrally with 0.03 cc. of a 1:10,000 dilution of infected guinea pig brain. Each of eight of these received 1 cc. of the serum by the intraperitoneal route forty-eight hours following the inoculation of virus. The remaining six mice were not treated with serum and were employed as the untreated controls.

One treated mouse became sick on the fifth day following the injection of virus and died three days later. Its brain and heart blood were cultured and were found to be free of bacterial contamination. Another mouse did not eat and appeared sick for two days following the serum administration but made a complete recovery. The remaining six treated animals did not show any signs of the infection. All the untreated control mice showed symptoms of the disease on the third day following exposure to the virus and died within eight days. In each case, except in one in which an air contaminant was encountered, the cultures of the specimens of heart blood were negative.

Fig. 4 (guinea pig 1, table 2).—Section of brain of guinea pig treated with serum when visibly ill; killed twenty-nine days after treatment was instituted; × 64.

Twenty days after inoculation with the virus the seven mice that were treated with serum were tested for immunity. Each was inoculated intracerebrally with 0.03 cc. of a 10^{-8} dilution (about a hundred times the minimum lethal dose) of Western type chick embryo virus. The dilutions were made in heart

12. Supplied by Dr. W. G. Malcolm of the Lederle Laboratories.
13. Supplied by the United States Bureau of Animal Industry.

infusion broth. All became infected and died, demonstrating that they did not become immunized as a result of the inoculations with virus and serum.

EXPERIMENT 2.—Fourteen Swiss mice were used in this experiment. Each was inoculated intracerebrally with 0.03 cc. of a 1:10,000 dilution of guinea pig brain virus. Eight of the animals were treated with serum when they showed visible signs of sickness; the remaining six were not given serum and constituted the untreated controls. All the mice became visibly sick within three to six days after injection of the virus. The mice that were considered to be visibly ill showed the following signs: slowness of movement, roughened coat, refusal of food, tremors and, in some cases, prostration and partial paralysis. The serum was administered intraperitoneally in 2 cc. doses.

Of the eight treated mice three died and five recovered completely. Of the three animals that died one received one dose of serum, the other two and the third three. Three of the mice that recovered were each given two doses of the serum, while each of the remaining two was given three doses. The surviving mice were tested for immunity twenty-four days later by intracerebral inoculation of each with 0.03 cc. of a 1:10,000 dilution of guinea pig brain virus. None of the animals became infected, showing that they had developed an active immunity as a result of having an attack of the disease from which they recovered following treatment with serum.

The control mice all became visibly sick in from three to four days after injection of the virus and died within ten days. Cultures of the heart blood of none of the animals that died in the course of this experiment showed any bacterial contamination.

EXPERIMENT 3.—Twelve guinea pigs were used in this experiment, of which each was inoculated intralingually with 0.4 cc. of a 1:100 dilution (at least a hundred times the minimum lethal dose) of infected guinea pig brain. The animals were divided into the following groups: four were given serum at the onset of the first rise in temperature, four were treated when they showed visible signs of the disease and four were not given serum and were employed as the untreated controls. The guinea pigs were adjudged visibly sick if they showed fever, roughened coats, refusal of food, slowness of movements, ataxia and in some instances partial paralysis.

The treatment consisted of inoculating the animals intraperitoneally with 10 cc. doses of the serum. The temperatures of the guinea pigs that were to be treated at the onset of fever were taken twice a day and of the others once a day. It is recognized that excessive handling is distinctly harmful to persons or animals with an infection of the central nervous system. To avoid this possibility temperatures of the animals were not taken after the commencement of serum therapy. The results of this experiment are shown in table 1.

As shown in this table, the four guinea pigs that were treated with serum at the onset of fever recovered after showing only slight evidence of the infection. It was necessary to give each of these animals only one 10 cc. dose of serum. Of the four guinea pigs that were treated when definite signs of illness were observed, three survived and one died. To effect recovery in this group, however, it was necessary to administer from 20 to 40 cc. of the serum to each of the animals. All the untreated control guinea pigs contracted the disease and died. Cultures were made of the heart blood of each animal that died and in every case they were negative.

The seven surviving guinea pigs were tested for immunity twenty days after exposure to the virus by injecting each intracerebrally with 0.25 cc. of a 1:10,000 dilution (about ten times the minimum lethal dose) of guinea pig virus. All four animals that were treated with serum at the onset of fever and one (guinea pig 5) of the group that was treated after characteristic symptoms were observed contracted the disease and died. The two remaining animals that were treated when visibly sick survived without showing any apparent signs of infection. They appeared to have acquired an active immunity from their exposure to the virus, indicating that infection had occurred.

EXPERIMENT 4.—In this experiment a commercial horse serum, produced by hyperimmunization of horses with chick embryo virus, was used for treatment. This serum, when tested for its protective value by the method described, was found to protect when undiluted serum was used, but only one third of the mice injected with the 1:10 dilution of serum survived. The higher dilutions did not show any protective properties. This serum was of low potency, apparently having only about one thousandth the protective value of our hyperimmune rabbit

TABLE 2.—*Experiment 5, Group 3 Treated with Hyperimmune Rabbit Serum When Visibly Ill*

	Guinea Pig 1		Guinea Pig 2		Guinea Pig 3		Guinea Pig 4		Guinea Pig 5		Guinea Pig 6		Guinea Pig 7		Guinea Pig 8		Guinea Pig 9		Guinea Pig 10	
Days	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms	Temperature	Symptoms
1	100.5	N	100.5	N	100.0	N	100.1	N	99.7	N	101.0	N	100.8	N	101.0	N	98.9	N	100.0	N
2	100.0	N	100.5	N	100.2	N	101.6	N	102.2	N	102.0	N	101.0	N	102.6	N	100.4	N	99.0	N
3	101.5	N	102.0	N	103.5										103.0	P	100.5	N	100.6	N
4	100.5	N	101.8	N	103.6	Pa	100.8	N	101.3	N	101.0	N	101.5	N	103.6					
					Died while serum was being given		102.2													
							102.2	P	98.6	N	101.3	N	101.4	N	104.4	S PR†	99.0	N	102.4	N
5	101.3	P	100.6	N	.....	..	102.8	PaM	100.3	P	102.8	S†	101.8	N	.....	S	101.7	S§	102.0	P
6	102.5	S	100.1	N	.....	..	Died before serum was given		101.5	P	101.7	Pa‡	101.9	P	.....	S	97.2	Pa†	101.6	P
7	102.0	PR†#	100.0	N	.....	..	.....	..	103.5	PR†	.....	M	103.5	S†	.....	S†	.....	Pa†#	101.0	S†
8	.....	Pa†#	101.8	N	.....	..	.....	..	.....	S	Dead		103.9	S‡	.....	P	.....	PR†#	99.5	S
9	.....	PR†#	100.5	N	.....	..	.....	..	.....	S‡	.....	..	.....	S	.....	N	Dead; pericardial hemorrhage		.....	S†
10	.....	S†#	100.7	N	.....	..	.....	..	.....	S‡	.....	..	.....	S‡	.....	N	.....	..	.....	S
11	.....	S†	100.7	N	.....	..	.....	..	.....	S‡	.....	..	.....	N	.....	N	.....	..	.....	N
12	.....	P	.....	N	.....	..	.....	..	.....	N	.....	..	.....	N	.....	N	.....	..	.....	N
13	.....	P	.....	N	.....	..	.....	..	.....	N	.....	..	.....	N	.....	N	.....	..	.....	N
14	.....	N	.....	N	.....	..	.....	..	.....	N	.....	..	.....	N	.....	N	.....	..	.....	N
15	.....	N	.....	N	.....	..	.....	..	.....	N	.....	..	.....	N	.....	N	.....	..	.....	N
16	.....	N	.....	N	.....	..	.....	..	.....	N	.....	..	.....	N	.....	N	.....	..	.....	N
17	.....	N	.....	N	.....	..	.....	..	.....	N	.....	..	.....	N	.....	N	.....	..	.....	N
18	.....	N	.....	N	.....	..	.....	..	.....	N	.....	..	.....	N	.....	N	.....	..	.....	N
19	.....	N	.....	N	.....	..	.....	..	.....	N	.....	..	.....	N	.....	N	.....	..	.....	N
20	.....	R	.....	R	.....	..	.....	..	.....	R	.....	..	.....	R	.....	R	.....	..	.....	R

†, 10 cc. of serum given intraperitoneally.
‡, 5 cc. of serum given intraperitoneally.
#, 5 cc. of physiologic solution of sodium chloride given subcutaneously.
§, 5 cc. of serum given intracardially.
N, no symptoms.
P, roughened coat, passive, not eating.
S, visibly ill.
Pa, paralyzed.
R, released.
PR, partial paralysis.
M, moribund.

serum. Consequently, as would be expected, the results of serum treatment in this experiment were not satisfactory.

Each of sixteen Swiss mice was injected intracerebrally with 0.03 cc. of a 1:10,000 dilution of guinea pig virus. In addition each of seven guinea pigs was injected intralingually with 0.4 cc. of a 1:100 dilution of the same virus. The mice were divided into the following groups: Four were treated with serum twenty-four hours and four forty-eight hours after inoculation with the virus, four when visible signs of infection could be observed and four were not treated and were used as controls. Of the guinea pigs five were treated with serum at the time they showed visible signs of the disease and two were used as untreated controls.

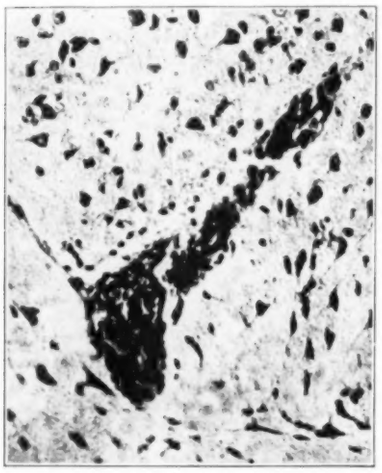

Fig. 5 (guinea pig 1, table 2).—Section of brain of guinea pig treated with serum when visibly ill; killed twenty-nine days after treatment was instituted; × 160.

The mice that were given 2 cc. of the serum twenty-four hours after exposure to the virus survived without showing any apparent signs of infection. All the mice to which serum was administered forty-eight hours after injection of the virus as well as those which were treated when visibly sick and the untreated controls became infected and died. Each of the treated mice in these two groups received about 5 cc. of the serum. Three of the treated mice lived seven days longer than the controls. However, it is not known whether or not this was due to the protective properties of the serum.

Four of the treated guinea pigs died and one recovered. Each of these animals received about 70 cc. of serum. Of the untreated controls one contracted the disease and died whereas the other did not become infected. The brain and heart blood of each animal that died were cultured and, with the exception of one guinea pig brain in which an air contaminant was encountered, were found to be free of bacterial contamination.

In this experiment, in addition to the serum treatment, dextrose solution was administered subcutaneously to the sick animals. Recently it has been reported that dextrose may be toxic to animals with certain virus infections.[14] Possibly this factor may have influenced the results of this experiment.

EXPERIMENT 5.—Thirty-three guinea pigs were used in this experiment, in which hyperimmune rabbit serum was again used. Each of thirty animals was injected intralingually with 0.4 cc. of a 1:50 dilution of a guinea pig brain virus and each of three was injected intracerebrally with 0.25 cc. of the same virus preparation. The animals that were inoculated intralingually were divided into three groups of ten each. In group 1 the animals were not treated with serum and they were used as controls on the infectivity of the virus, in group 2 treatment with immune serum was started at the onset of fever and in group 3 the animals were given serum when they showed visible signs of the infection. The intracerebrally inoculated guinea pigs were employed to establish the virulence of the virus.

The treatment with immune serum consisted of administering the serum intraperitoneally in 10 cc. doses. In addition, for the purpose of keeping up the body fluids physiologic solution of sodium chloride was given in a few cases by subcutaneous inoculation. In a few instances in which the guinea pigs were very sick, about 5 cc. of serum was injected either intravenously or intracardially in order to make the antibodies available more quickly.

14. Hoyt, Anson; Holden, Margaret, and Rawson, Ruth A.: Decreased Tolerance of Mice to Intraperitoneal Glucose Injections in Certain Neutropic Virus Infections, Proc. Soc. Exper. Biol. & Med. **42**: 332 (Oct.) 1939.

In the control group of animals eight contracted the disease and died, while two did not show any apparent infection. Eight of the guinea pigs in group 2 became infected and two did not. The temperature of these animals was taken in the morning and late in the afternoon, and as soon as a rise was observed 10 cc. of serum was administered. All the guinea pigs had a fever within a period of from three to five days following inoculation. Following serum treatment the condition of each animal was observed closely, and if the animal showed further signs of infection more serum was given. Of the eight guinea pigs treated, two showed complete recovery following the administration of the 10 cc. of serum. It was necessary to give four animals an additional 5 cc. One guinea pig at the onset of fever also showed signs of being visibly sick. It was given 10 cc. of serum but died within twelve hours. The remaining animal was killed while serum was being injected intracardially. Thus, of the eight animals treated, six recovered, one died of the infection and one suffered a traumatic death.

In group 3, nine guinea pigs contracted the disease while one escaped infection. Of the nine infected animals five were treated with serum successfully, one was killed while serum was being injected intravenously, one died before treatment could be instituted and one died after it was treated with 15 cc. of serum. One animal died four days after an intracardial injection of serum and when it had apparently recovered from the disease. On autopsy, it was found to have suffered from a pericardial hemorrhage. The results of treatment in group 3 are shown in table 2.

The three control guinea pigs that were inoculated intracerebrally became infected and died within six days. The cultures of the heart blood and brain of each animal that died in the course of this experiment were free from bacterial contamination.

Thirty-three days after the beginning of the experiment we tested four of the recovered guinea pigs for immunity by inoculating each intracerebrally with 0.25 cc. of a 1:1,000 dilution (about a hundred times the minimum lethal dose) of guinea pig brain virus. Two guinea pigs that recovered after treatment with serum at the onset of fever and two animals that recovered following serum treatment when they were visibly sick were subjected to this test. The virulence of the virus was tested by the simultaneous injection of two normal guinea pigs intracerebrally. Of the four animals tested for immunity, one that was treated with serum at the onset of fever contracted typical signs of encephalomyelitis and died. None of the remaining guinea pigs became infected, showing that the disease had progressed sufficiently in these animals to produce active immunity. The intracerebrally inoculated animals became infected and died. The summary of the results

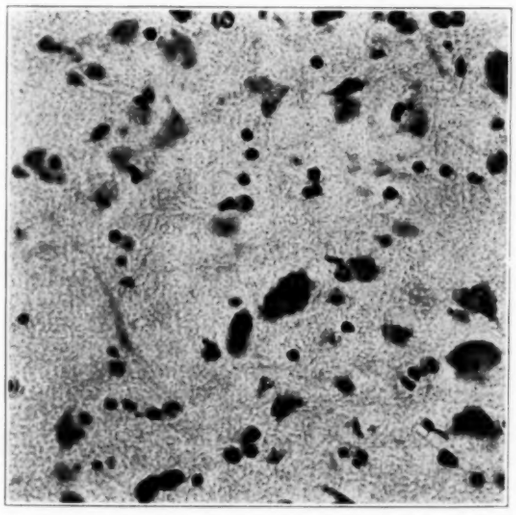

Fig. 6 (guinea pig 1, table 2).—Section of brain of guinea pig treated with serum when visibly ill; killed twenty-nine days after treatment was instituted; × 400.

of the experiments in which rabbit hyperimmune serum was used for treatment is shown in table 3.

Histopathologic studies [15] were made of the brains of selected animals to determine whether lesions had been present when serum therapy was instituted and to determine whether repair had taken place in the brain tissues of the serum treated guinea pigs. For this purpose two animals that were treated at the onset of fever were killed twelve days after injection of the serum and two of the same series were killed twenty-eight days after serum treatment. Of the animals that were treated with serum after visible illness, two were killed twelve days after the first injection of serum and one was killed twenty-nine days after serum treatment had been instituted. For comparison, sections were made of the brains of six control animals that did not receive serum and died and of two animals that died following injection of serum. The histopathologic studies are here described.

MICROSCOPIC STUDIES

Untreated Guinea Pigs.—Microscopic sections of brains from the control animals disclosed a diffuse and marked inflammatory and degenerative process. There was a mild focal meningeal infiltration of lymphocytes. In some sections there was massive cellular infiltration extending along the fissures (fig. 1). Perivascular infiltration with monocytes and lymphocytes was variable in degree but almost always present. Some proliferation of adventitia could be detected. There was rather diffuse and widespread degeneration of the neurons, which appeared in varying stages of necrosis. In some sections there was focal neuronal necrosis with a marked interstitial cellular reaction consisting of degenerating polymorphonuclear cells, lymphocytes and also glial cells.

Guinea Pigs Treated at Onset of Fever; Killed Twelve Days Later.—A few focal areas of mild lymphocytic meningeal infiltration were visible. The perivascular infiltration, although definite, was minor in degree, consisting of a few loose lymphocytes to a necklace encirclement one cell layer in thickness. Occasional ghost and pyknotic neuronal cells were present.

Guinea Pigs Treated at Onset of Fever; Killed Twenty-Eight Days Later.—These slides were similar to those of the preceding section with the pathologic changes somewhat less evident.

Guinea Pigs Treated When Visibly Sick; Killed Twelve Days Later (table 2, guinea pigs 5 and 8).—There was marked evidence of inflammatory reaction in these sections. There was focal meningeal infiltration with lymphocytes extending down the fissures. Perivascular infiltration and adventitial and intimal proliferation was quite prominent (fig. 2). Many neuronal cells were mere ghosts. Others showed vacuolization or pyknosis with loss of nuclei and irregular outlines (fig. 3). Neuroglial proliferation was evident.

Guinea Pig Treated When Visibly Sick; Killed Twenty-Nine Days Later (table 2, guinea pig 1).—Sections from this animal showed definite evidence of a subsiding inflammatory and degenerative process. Focal infiltration with old lymphocytes could be found (fig. 4). There was a moderate perivascular infiltration of heavily stained mononuclear cells (fig. 5). Adventitial and intimal proliferation of the arterioles was also present. There was little interstitial lymphocytic infiltration, and no polymorphonuclear cells were seen in any of the sections. Degenerated neurons, some pyknotic, others showing vacuolization or disintegration (fig. 6) and some microglial proliferation, were to be seen.

SUMMARY AND CONCLUSIONS

Western equine encephalomyelitis can be treated with hyperimmune rabbit serum with practically complete success in mice forty-eight hours after injection of virus and in guinea pigs after the appearance of the first sign (fever) of the disease. About two thirds of the animals treated with serum when the infection has progressed to the point at which visible signs of the disease manifest themselves can be saved. The fatality in control animals not receiving treatment is 100 per cent.

15. The Pathology Department, Michael Reese Hospital, Chicago, aided in preparing the slides and photomicrographs and in the interpretation of the histopathologic appearances.

Probably a higher percentage of animals could have been treated successfully with serum if the earlier visible signs of infection were more striking. Also because of the impossibility of watching the animals twenty-four hours a day in some cases animals failed to receive serum as soon as visible signs of infection appeared. Owing to these facts, as our protocols show, animals were sometimes treated only after onset of paralysis or even when they were moribund. Most of the animals treated when completely prostrated died.

Proof that specific infection actually existed at the time serum therapy was instituted is supplied by three lines of evidence: The disease continued to progress in some animals, causing death, in other cases the disease progressed for a few hours after serum therapy was begun, and some of the animals appeared to be moribund before recovery began. The histopathologic studies of recovered animals that were killed two and four weeks after recovery demonstrate that widespread damage of the tissues of the central nervous system had occurred but that the inflammatory reaction and destructive changes were receding when the animals were killed. This is confirming evidence that the virus was proliferating in and damaging the brain, and apparently the serum arrested the progress of the infection. Finally, the fact that some of the survivors among the animals treated after onset of symptoms were immune to a subsequent intracerebral injection of virus, whereas those treated earlier were not, indicates that the infection had proceeded far enough to produce an active immunity.

TABLE 3.—*Summary of Results After Treatment with Hyperimmune Rabbit Serum*

Experiment Number and Animals Used	Treated 48 Hours After Virus Injection	Treated at Onset of Fever	Treated When Visibly Ill	Untreated Controls
1 Swiss mice.....	1/8*	—	—	6/6
2 Swiss mice.....	—	—	3/8	6/6
3 Guinea pigs.....	—	0/4	1/4	4/4
5 Guinea pigs.....	—	1/7	1/6†	8/8
Number dead after treatment.....	1	1	5	—
Total animals used....	8	11	18	24
Per cent recovery after treatment.....	87.5	90.9	73.3	0.0

* Numerator equals the number of animals dead after serum treatment; denominator equals the number of animals used in experiment.
† Not including one delayed death from pericardial hemorrhage.

A commercial serum, produced by immunization of horses, which had a potency only about 0.1 per cent as high as that of our rabbit hyperimmune serum, had no beneficial effect on the course of the infection in animals treated after visible signs of the disease appeared. It also failed to protect mice when administered forty-eight hours after injection of virus but was effective when given twenty-four hours after the injection. It is believed that this experiment serves as a good control. Furthermore, it emphasizes the importance of potency and dosage of therapeutic serums.

It is believed that the reason for the success of these studies is that adequate dosage (in terms of antibodies) was employed. The use of rabbit serum, which is believed to have smaller antibody molecules and which probably penetrated to the infected tissues more rapidly, may also have had a favorable influence on the treatment.

Although the number of animals used in these experiments was relatively small, it is believed that the results are significant because of their consistency and because

they receive strong support from the histopathologic examination and the results of the immunity tests. Further studies are being conducted at this time.

Evidence has been presented from the literature that other virus diseases have been successfully treated with serum. However, as far as we are aware, this is the first instance in which evidence from controlled studies of the successful treatment of a virus disease which causes its chief damage in the central nervous system has been presented.

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VITAMIN DEFICIENCIES IN DIARRHEAL STATES

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In the light of present knowledge of nutrition made available by the recent discovery and clinical trial of synthetic vitamins, it is well to appraise the role of disorders other than malnutrition itself which predispose to or precipitate nutritional deficiency syndromes. We know that most deficiency diseases result from a combination of adverse circumstances rather than from a single one. This is well illustrated in cases of so-called secondary deficiencies which follow organic disease. We have been particularly interested in the vitamin B complex factors and in the disease states which result from an inadequacy or complete absence of these factors.

Many circumstances may operate in preventing a person from receiving an optimal amount of the vitamins which he requires. Not only may his intake be inadequate, but his powers of assimilation and utilization of these substances may be impaired. Thus diseases and disorders of the alimentary tract play an important part in the development of deficiency states. The present paper is concerned with the role of chronic diarrhea in the production of such syndromes as pellagra, beriberi and riboflavin deficiency.

The medical literature contains many case reports of vitamin deficiency syndromes which complicated diseases of the alimentary tract. One of the earliest was reported by Rolph,[1] who noted pellagra in a patient with carcinoma of the stomach. Joyce and Seabrook[2] were the first to call attention to rectal stricture as a forerunner of pellagra. Turner[3] too has reported examples of jejunal and ileac stenosis, amebic dysentery and rectovaginal fistula as other gastrointestinal disorders which might eventuate in pellagra. Barnes[4] recorded a similar complication of chronic ulcerative colitis. Yang and Hu[5] described a case of beriberi associated with amebic dysentery, ulcerative colitis and operations shortcircuiting the alimentary canal. Both Strauss[6] and Stannus[7] have given comprehensive reviews of the role played by diseases of the intestine in "conditioning" deficiency disease.

MECHANISMS BY WHICH DIARRHEA MAY LEAD TO DEFICIENCY STATES

1. *Increased Loss of Ingested Vitamins.*—(*a*) In chronic diarrhea the most important loss of vitamins and other food constituents is the direct result of the rapid transit of ingested materials through the alimentary tract. In a number of our patients who developed pellagra, neuritis or cheilosis as a sequel of chronic diarrhea we found that dyes ingested with the food usually appeared in the stool within four hours, and occasionally in less than one hour. It is obvious that this speeding up of intestinal transport does not permit adequate absorption of the food, even if digestion is normal.

(*b*) In most disorders of the alimentary tract, however, there is a decrease or even absence of some digestive juices so that proper enzymatic attack on the food does not occur.

2. *Decreased Absorption of Vitamins.*—In addition to these primary obstacles there are frequently organic changes in the intestine which may impede absorption. There is evidence to show that many simple sugars, dextrose, galactose and lactose, are not absorbed normally in deficiency states.[8] It seems probable that the inflamed, scarred or atrophic bowel in chronic diarrhea absorbs poorly.

3. *Impairment of Possible Vitamin Synthesis in the Intestine.*—A consideration not yet studied in man is the possibility that certain vitamins, or even the enzyme systems in which they occur in the body, are formed in the intestine through the agency of bacterial synthesis. It is known that colon bacilli can synthesize nicotinic acid (Knight). In like manner bacteria can form other vitamins from primitive materials containing carbon, nitrogen, hydrogen and oxygen.[9] There is evidence that sheep normally synthesize several members of the vitamin B complex from simple food elements in the intestine.[10] It is not too novel to suppose that normal bacterial residents in the alimentary canal may play a role in synthesizing vitamins. Whether this is important or not is speculative. In certain infections, notably those of the dysentery bacteria, it is conceivable that the organisms in the intestine use or destroy a large part of the vitamin content of ingested food and leave an inadequate amount for the needs of the host.

4. *Decreased Phosphorylation of Vitamins.*—Phosphorylation of some of the products of digestion ordinarily takes place in the intestinal canal. It is probable that this function is impaired in any diarrhea of long duration.

5. *Additional Factors Leading to Deficiency States in Chronic Diarrhea.*—Individuals with some forms of diarrhea may have a considerable increase in metabolism owing to the fever associated with infection. The advent of cramping pains, anorexia, nausea and vomit-

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2. Joyce, T. M., and Seabrook, D. B.: Stricture of the Rectum as an Indirect Cause of Pellagra, Northwest Med. **24**: 254 (June) 1925.

3. Turner, R. H.: Pellagra Associated with Organic Disease of the Gastrointestinal Tract, Am. J. Trop. Med. **9**: 129 (March) 1929.

4. Barnes, J. M.: Typical Pellagra Syndrome Developing in a Patient with Chronic Ulcerative Colitis While Under Hospital Treatment, Ann. Clin. Med. **4**: 552 (Jan.) 1926.

5. Yang, C. S., and Hu, C. K., cited by Stannus.[7]

6. Strauss, M. B.: The Role of the Gastrointestinal Tract in Conditioning Deficiency Disease, J. A. M. A. **103**: 1 (July) 1934.

7. Stannus, H. S.: Pellagra-like Conditions in Warm Climates, Trop. Dis. Bull. **33**: 729 (Oct.) 1936.

8. Groen, Juda: The Absorption of Glucose from the Small Intestine in Deficiency Disease, New England J. Med. **218**: 247 (Feb. 10) 1938. Althausen, T. L.: A Test for Intestinal Absorption, Am. J. Digest. Dis. **6**: 544 (Oct.) 1939.

9. Koser, S. A., and Saunders, Felix: Accessory Growth Factors for Bacteria and Related Micro-Organisms, Bact. Rev. **2**: 99 (Dec.) 1938.

10. McElroy, L. W., and Goss, Harold: Report on Four Members of the Vitamin B Complex Synthesized in the Rumen of the Sheep, J. Biol. Chem. **130**: 437 (Sept.) 1939.

ing may put an effective blockade on the very source of supply by reducing the intake of food. Any factor which has previously undermined the nutritional status of an individual will increase his liability to a deficiency syndrome in the event of an outbreak of diarrhea. The relationship of these underlying mechanisms is portrayed in table 1.

TABLE 1.—*Disturbance in Vitamin Balance Leading to Deficiency Diseases in Diarrheal States*

	Decreasing Supply			
	Increased Loss	Decreased Assimilation	Decreased Intake Anorexia Vomiting	Increasing Demand: Increased Metabolism
Stricture and stenosis	+	±	+	−
Intestinal obstruction	+	+	+	±
Fistulas	+	+	±	−
Intestinal parasites	±	+	−	−
Colitis	+	+	±	±
Dysentery	+	+	+	+
Functional diarrhea	+	±	±	±
Diarrhea or pellagra	+	+	+	−

ROLE OF THE VITAMIN B COMPLEX IN INTESTINAL FUNCTION

There is much evidence to support the opinion that some of the vitamin B complex factors are important for normal intestinal function in animals. The literature on this problem has been reviewed by Borsook, Dougherty, Gould and Kremers.[11] They adduced evidence that many of the chronic digestive complaints in a large series of patients could be relieved by the addition of a dietary supplement containing a high concentration of vitamin B complex factors. Evidence for basic function of thiamine in intestinal motility is not conclusive. In experimental thiamine deficiency, Cowgill[12] observed hypochlorhydria and loss of tone in the gastric musculature. Vorhaus, Williams and Waterman[13] reported a small series of cases in which constipation was relieved following the administration of large doses of thiamine.

In a study on the effect of an intravenous injection of from 10 to 25 mg. of nicotinic acid, we[14] noted that in four of eight subjects examined under the fluoroscope with barium sulfate in the stomach no change could be demonstrated, but the other four had a definite increase in the depth of the peristaltic concentration rings of the stomach. Two of them had severe cramps associated with generalized increase in gastric tonus, considerable decrease in the size of the stomach, and complete cessation of all gastric movement for a minute. After resumption of gastric activity, the contraction waves rose much higher toward the cardiac end than before the injection and were much deeper than they were prior to the administration of the drug. This observation was extended by Crandall, Chesley, Hansen and Dunbar,[15] who noted hypermotility and irregularity in the intestinal pattern with areas of atony interrupted by areas indicating spasm in B deficient dogs. They concluded "that the P-P factor (nicotinic acid, nicotinamide or any carboxypyridine derivative capable of replacing these in the diet) is essential to the maintenance of normal gastrointestinal motility and that absence of this factor leads to motor dysfunction of the intestinal tract prior to the appearance of the usually accepted deficiency symptoms." They believed the whole B complex to be more effective than is nicotinic acid alone. Thiamine and riboflavin were inactive under the conditions of their experiment.

Thus it is clear that some elements of the vitamin B complex are of great importance in normal alimentary function. This is again demonstrated in the relief of the diarrhea of endemic pellagra by nicotinic acid. When such a diarrhea is not treated, a pernicious cycle begins. Many other vitamin B complex factors, already poorly supplied by the diet, are lost and diagnostic signs of a deficiency of thiamine or riboflavin may appear. Nicotinic acid usually relieves the diarrhea and with the restoration of normal alimentary function the related deficiencies often clear up if they are not too far advanced.

DIARRHEA IN INFANTS AND CHILDREN

There has been little study of the part played by diarrhea in predisposing infants and children to deficiency diseases. Spies, Walker and Woods[16] have emphasized the frequency of nicotinic acid deficiency in summer diarrhea. Where pellagra is endemic it may be impossible in some cases to determine whether a diarrhea is primarily an infection or a deficiency disease. Diagnostic cutaneous lesions are rare in infants,

TABLE 2.—*One Hundred Cases with Diarrhea Leading to Deficiency Diseases*

	No. of Cases
1. Pellagra (nicotinic acid deficiency)	36
2. Summer diarrhea in infants and children	13
3. Intestinal obstruction (partial), carcinoma of rectum, colon, stomach	10
4. Stricture (lymphopathia) *	8
5. Bacillary dysentery	3
6. Nursing infants whose mothers have diarrhea (pellagra)	3
7. Sprue	2
8. Ulcerative colitis	2
9. Intestinal tuberculosis	2
10. Gastric neurosis	2
11. Thyrotoxicosis	2
12. Gastrocolic fistula	1
13. Adhesions (postoperative)	1
14. Food poisoning	1
15. Undiagnosed	14
Total	100

In most cases included above there were additional factors predisposing to deficiency disease. Pregnancy, childbirth or lactation occurred in thirty-three, infections (not included above) twenty-eight, operations fifteen, alcoholism seven, pernicious anemia two, and there were many other factors.

* Five of these patients had a colostomy.

but chemical tests and the therapeutic response leave no doubt that a deficiency of nicotinic acid often dominates the picture. As an interesting corollary on the effect of diarrheal states, we have seen pellagra in three nursing infants whose mothers were on a grossly inadequate diet during pregnancy (table 2). When a diarrhea occurred in the mother, the child developed glossitis and diarrhea which cleared up when the baby was put on a formula with a supplement of nicotinic acid.

11. Borsook, Henry; Dougherty, Paul; Gould, A. A., and Kremers, E. D.: The Vitamin B Complex and Functional Chronic Gastrointestinal Malfunction: A Study of 227 Cases, Am. J. Digest. Dis. **5**: 246 (June) 1938.

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REPORT OF CASES

Because of the complexity of the relationship between chronic diarrheas and vitamin deficiency diseases, several cases will be presented to illustrate different aspects of the problem:

Case 1.—*Pellagra and riboflavin deficiency in a case of rectal stricture.* C. D., a Negro woman aged 34, was relieved of the glossitis and diarrhea of pellagra by treatment with nicotinic acid in the Hillman Hospital in the spring of 1938. This was her first attack and followed the prolonged use of liquid petrolatum several times daily to facilitate the bowel movements impeded by a rectal stricture. There was no change in the diet during the period she was followed. Her food intake was never good either in quality or in quantity. She was followed in the clinic during 1939, and another outbreak was controlled with nicotinic acid (300 mg. a day for several weeks). In February 1940 a colostomy was performed for the stricture. The wound was only partially healed when she was seen on April 24. She had a severe cheilosis. She was observed for a period of two weeks, during which the diarrhea persisted unchecked with from five to ten loose stools a day. She was then given paregoric 5 cc. from two to four times a day for five days. The diarrhea was controlled and within two weeks the mouth lesions healed and her weight increased from 98 (44.5 Kg.) to 107 pounds (48.5 Kg.). The operative wound healed. She failed to return for ten days and the diarrhea recurred in severe form. The cheilosis then reappeared and she developed a painful glossitis. These were relieved by riboflavin and nicotinic acid.

A long period of disordered intestinal function occasioned by a rectal stricture and abuse of liquid petrolatum predisposed this patient to the development of pellagra. She was treated successfully with nicotinic acid, but an operation soon precipitated another attack of the disease. Recovery followed the partial restoration of normal bowel function. Later the development of a chronic diarrhea eventuated in a relapse of the cheilosis. The signs of deficiency disease disappeared after the diarrhea was checked by paregoric. When paregoric was stopped, the diarrhea recurred and the lesions once more reappeared. This sequence demonstrates the role of diarrhea in precipitating deficiency diseases. It also shows that, if diarrhea is the prepotent cause of the deficiency state, cure of the diarrhea may relieve the deficiency without other therapy. In this case colostomy reduced the absorbing area of the bowel and decreased the margin of safety, which was already small owing to the poor diet of the patient.

Case 2.—*Riboflavin deficiency relieved with large oral doses of riboflavin while diarrhea continued.* A. L., a Negro aged 54, developed a diarrhea in December 1939, which was still present when he was first examined on May 14, 1940, three weeks after admission to the urologic service of the Hillman Hospital. His diet was very meager and his weight had fallen from 140 (63.5 Kg.) to 90 pounds (41 Kg.) in five months. He had a granulomatous lesion of the rectum, which had reduced the function of the sphincter. During January he noted a dermatitis of the elbows and legs, which was, however, healing and almost well by May. Pains in his legs and burning and paresthesia of the skin began in February. One week before he was examined, his eyes began to hurt and sores appeared at the angles of the mouth. The patient exhibited a variety of lesions. The pellagrous skin lesion was healed and showed thickened pigmented areas on the elbows, shins and feet. The eyes were inflamed, the scleras muddy and the conjunctival vessels injected, particularly in the circumcorneal area. Photophobia was moderate. There were marked arcus senilis and irregular corneal opacities within this ring. There was an unsustained horizontal nystagmus. The mouth showed fearful caries, snags and gum retraction. The tongue was coated but not unusually red. At both angles of the mouth there were macerated whitish lesions surrounding a shallow fissure. The pink color of the buccal mucosa spread out over part of the lip which is normally brown and a new line of demarcation appeared. The lips were mottled and there was some cracking and peeling of the superficial layer. There was pain on pressure over the lower part of the legs and the feet and some hyperesthesia of the hands. The knee jerks were very weak and the ankle jerks absent. The heart was regular and a tic-tac rhythm was present. A rectal stricture and granuloma of the penis completed the picture. He was given riboflavin orally, 5 mg. three times daily, for five days during which the diarrhea was not treated. In spite of the continuation of from six to eight bowel movements a day, the cheilosis healed during this period. The conjunctival injection and photophobia disappeared and the patient stated that he felt much improved. Determination made on the riboflavin content of the blood revealed a change from 0.37 to 0.58 microgram per cubic centimeter of whole blood before and four days after treatment was begun.

In this case it was possible to relieve the lesions by fairly large oral doses of crystalline riboflavin even during a continuous diarrhea. After therapy the riboflavin concentration in the blood showed an increase. It seems clear, however, that much of the material given was wasted. It is probable that smaller parenteral doses would have been satisfactory also. His other deficiencies were relieved by nicotinic acid and thiamine.

Case 3.—*Deficiency in "colitis."* J. T. M., a white man aged 35, was nervous and high strung. He had a nondescript array of gastric complaints characterized by burning of the stomach, gas, belching, constipation and headache. His diet was barely adequate because he restricted himself owing to his stomach complaints. In February 1939 he had two attacks of "colitis" characterized by a mucous diarrhea, abdominal cramps, tenesmus and some decrease in appetite. These attacks lasted about ten days each. After the second, he began to develop a sore red tongue and cheilosis. He had insomnia, nervousness and considerable burning of the eyes. All signs and symptoms, except for constipation and vague gastric complaints, had cleared up by the end of March, one month after the diarrhea ceased. There were no recurrences of the oral lesions during the remainder of the year. When seen April 10, 1940, he had no sign of any deficiency disease. For experimental purposes he was given thyroid substance (Armour) 1 grain (0.065 Gm.) daily for two weeks and experienced some subjective improvement. The dose then was increased to 2 grains (0.13 Gm.) daily. Sixteen days later he was experiencing an increase in bowel movements to five or more a day. He developed cheilosis and a sore red tongue. Since this study was complicated by an intercurrent cold, the thyroid was discontinued. The lesions cleared up during the next week.

This case, in which the borderline diet provided a perilous margin of safety, reveals that an acute colitis may be the episode which brings out the latent deficiency state. An attempt to produce a diarrhea was successful, and this was followed by an outbreak of glossitis and cheilosis. Whether thyroid acted to increase the metabolism is uncertain but in some other cases in which this treatment was given there was no relapse.

Case 4.—*Failure of vitamin therapy to relieve the diarrhea of advanced ulcerative colitis.* M. T., a Negro woman aged 53, was first observed with signs of pellagra in the spring of 1938. Her initial attack occurred in 1924 and there had been several recurrences. Early in March 1938 she developed a diarrhea which, with a few short intermissions, continued until her death. During the spring and early summer of 1939 she was treated with nicotinic acid from 100 to 200 mg. daily and had complete relief of all her symptoms except the diarrhea, which however decreased in severity. She received no treatment during the next fall and winter while the diarrhea continued, and she had from ten to twenty watery stools daily. She was admitted to the Hillman Hospital March 20, 1940, in an extreme state of dehydration and malnutrition. Her weight had fallen from 152 (69 Kg.) to about 75 pounds (34 Kg.) in eight

months. She had a severe glossitis, stomatitis, dermatitis, peripheral neuritis and cheilosis. Laboratory studies revealed red blood cells of 2.7 million, hemoglobin 4.6 Gm., hematocrit 17 mm., serum protein 4.76 with fibrin 0.21, albumin 1.72 and globulin 2.83 Gm. per hundred cubic centimeters. Large intravenous and oral doses of nicotinic acid, thiamine, riboflavin and vitamin B_6 were effective in relieving the signs of glossitis, stomatitis, neuritis and cheilosis, but the diarrhea persisted. A high caloric, high protein diet was given, and repeated transfusions were of no avail as the patient lapsed into a state of vascular collapse. Adrenal cortex extract was given but was of only temporary value. After nineteen days of exceedingly painstaking treatment the patient died. An autopsy revealed an extensive ulcerative colitis with large areas of sloughing, necrosis and gangrene, especially in the sigmoid and rectum. The liver was fatty. No abnormality was seen in the adrenals. There was an early miliary tuberculosis in the peritoneum.

The clinical evidence of pellagra, beriberi and riboflavin deficiency disappeared following large parenteral doses of nicotinic acid, thiamine, vitamin B_6 and riboflavin. The diarrhea, after a short period of improvement, relapsed into the severe type, which persisted until her death. In every case of pellagra in which nicotinic acid has not relieved diarrhea we have found some organic lesion to account for the failure. Many persons with severe diarrhea, if seen early enough, are restored to normal bowel function by nicotinic acid, as was done in this case for a period of time. It seems probable that in this case the initial diarrhea aggravated the deficiency of nicotinic acid. This in turn may have increased diarrhea further and led to a deficiency of thiamine and riboflavin.

TREATMENT

1. *General Measures.*—Whenever diagnostic evidence of a vitamin deficiency disease appears in a patient with chronic diarrhea, it is imperative to institute emergency measures. It is theoretically sound to eliminate the diarrhea at once, but some patients first must be treated for the deficiency state if it is more critical than the underlying disease. In such instances, concentrates (liver extract and brewers' yeast) and crystalline vitamins may be of great value. As soon as the deficiency is controlled, the diarrhea should be investigated and relieved whenever possible.

Absolute rest in bed, preferably in a hospital providing expert nursing and dietary care, is the first requirement. Sedatives, camphorated tincture of opium (paregoric) or preparations of bismuth may be helpful. A high protein, 4,500 caloric diet including frequent supplements of milk and eggnog should be given. Replacements should be made to compensate for any food lost because of excessive vomiting or diarrhea. Solid food should be taken as soon as it can be tolerated. Attention should be paid to restoration of fluid, electrolytes, protein and all other essential substances of which the body may be depleted. In addition to specific therapy with crystalline vitamins, it is well to give concentrates of yeast or liver extract because they contain as yet unidentified factors in the B complex which may be needed.

2. *Specific Therapy—Nicotinic Acid.*—Parenteral injection of nicotinic acid amide should be given as soon as the diagnosis of pellagra is established or even suspected. This compound does not produce flushing, and large doses (250 mg.) may be given intravenously.[17] We attempt to give the patient 1,000 mg. the first day, 500 mg. daily for a week, and smaller doses thereafter. Repeated small oral doses (100 mg.) are satisfactory if the diarrhea is not severe. Since the exact requirement varies, it is desirable to use large doses. This regimen usually improves the patient to the point where the diet can be taken and a thorough investigation of the cause of the diarrhea is possible.

17. Bean, W. B., and Spies, T. D.: A Study of the Effects of Nicotinic Acid and Related Pyridine and Pyrazine Compounds on the Temperature of the Skin of Human Beings, Am. Heart J. **20**: 62 (July) 1940.

THIAMINE

Intravenous injections of thiamine hydrochloride, 50 mg. daily in from two to four doses, control the specific deficiency. Smaller doses, from 10 to 25 mg. daily, will control mild cases. If pain is the chief manifestation, it is usually relieved in a spectacular way. Organic changes respond slowly and it may be necessary to continue therapy for many weeks, but results are not encouraging in advanced cases. Wet beriberi is not frequently encountered in chronic diarrheas. Therapy in such cases should include, in addition to thiamine, all the general measures for relief of congestive failure. Digitalis is of little value. Serum protein should be determined to see whether hypoproteinemia is present. If so, it may be corrected by transfusion of blood or plasma if a high protein diet cannot be taken at once.

RIBOFLAVIN

Parenteral injection of from 2 to 5 mg., or ingestion of twice that amount, will relieve most cases. Because of the relative insolubility of riboflavin, oral therapy is usually advised. Cheilosis is an indolent lesion and responds slowly, usually only after several days (from four to seven) of treatment. It has not been demonstrated that a deficiency in riboflavin is fatal to man, but there is no question that the vitamin is of great value in many cases, even when no lesions are present.

VITAMIN B_6

The occasional response to vitamin B_6 among endemic pellagrins suggests that a deficiency of vitamin B_6 may occur in cases of chronic diarrhea. The dose we have used is from 20 to 50 mg. intravenously.

PANTOTHENIC ACID

The indications and dosage for pantothenic acid have not yet been established for human beings.

OTHER VITAMINS

Treatment of deficiencies in vitamins A, C, E and K follows the principles already outlined.

SUMMARY AND CONCLUSIONS

In an area of endemic pellagra, beriberi and riboflavin deficiency we have encountered 100 individuals who developed such syndromes as a complication of chronic diarrhea. This number constitutes about 10 per cent of the patients with deficiency diseases.

Chronic diarrhea predisposes to the development of deficiency syndromes by causing increased loss and decreased absorption of vitamins. If the diarrhea is relieved even without vitamin therapy, the secondary deficiencies usually improve.

In deficiency diseases which occur as sequels of a chronic diarrhea, parenteral injections of crystalline vitamins are essential in proper treatment but do not take the place of a high protein, high caloric diet. Nicotinic acid amide (from 500 to 1,000 mg. daily), thiamine hydrochloride (from 10 to 50 mg. daily) and riboflavin (from 2 to 10 mg. daily) will relieve specific deficiencies in most cases.

THE CLINICAL VALUE OF VITAMIN K

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As vitamin K has only recently been discovered, and synthetic substances with vitamin K activity are at the present time receiving intensive study, our knowledge as to the clinical value of this vitamin is as yet very limited. Although its effect on the hemorrhagic diathesis in chicks on a vitamin K deficient diet has been fairly well worked out, its therapeutic use with patients is largely an unsolved problem. A few disorders with K deficiency are now well recognized; its relationship to a number of others seems probable, and it is possible that it may be of some importance in certain hemorrhagic conditions which have received little or no study up to the present time. Largely on empirical grounds it has been stated that this vitamin is of no value in a number of conditions in which free bleeding may occur.

Clinical studies have been advanced to some extent by the development of certain laboratory tests indirectly indicating vitamin K deficiency. However, when the vitamin first became available commercially the chief source was an alfalfa extract, although putrefactive bacteria were also utilized, and during this time therapy was considerably limited by the instability of the early products and the cost of their production. More recently a number of synthetic compounds with vitamin K activity have been discovered.[1] These are readily produced and are stable and have made possible the rapid advancement in knowledge during the past year because a larger number of cases could be treated.

Of necessity the early reports dealing with vitamin K deficiency and its clinical management resulted in an incomplete understanding concerning the use of the vitamin and caused it to be tried in a great many conditions in which there was absolutely no positive indication for its administration. Its actual clinical value at present may well be presented under four different headings:

1. Those conditions in which its use is positively indicated.
2. Conditions in which it is probably of value, at least in certain cases.
3. Conditions in which it may possibly prove valuable but have as yet been insufficiently studied.
4. Disorders in which it has proved unsuccessful.

DISORDERS DEFINITELY ASSOCIATED WITH VITAMIN K DEFICIENCY AND WHICH ARE BENEFITED BY VITAMIN K THERAPY

Disorders definitely associated with vitamin K deficiency and which are benefited by vitamin K therapy are relatively rare but have been reasonably well defined. They may be divided into two general groups. In the first there is an absence of bile in the intestinal tract and this interferes with the normal absorption of the fat soluble vitamin K. This is most commonly encountered in cases of obstructive jaundice due to stones, cancer, stricture and the like and may also be present in patients with biliary fistulas and long standing duodenal drainage.[2] A similar situation may arise in patients with acute and severe hepatitis, such as an acute yellow atrophy of the liver and in yellow fever when no bile reaches the common duct.

The second important type of disorder in which vitamin K deficiency has been clearly recognized is the hemorrhagic disease of the newborn and the tendency of premature infants to bleed. These conditions are associated with prothrombin deficiency and are rapidly alleviated by vitamin K therapy.[3]

DISORDERS IN WHICH VITAMIN K DEFICIENCY MAY OCCUR BUT THERAPY IS NOT CONSTANTLY EFFICACIOUS

The group of disorders in which vitamin deficiency may occur but in which treatment is not constantly efficacious may be divided into four types. In the first a nutritional deficiency would depend on a complete lack of food or a lack of food containing vitamin K.[4] Even under such conditions it is difficult to understand how true K deficiency could occur, as this vitamin is known to be manufactured by putrefactive bacteria constantly present in the intestine. On a similar basis, deficiency might occur from an obstruction in the esophagus or at the pyloric end of the stomach. It would be more likely to develop in an obstruction high in the jejunum, as occasionally occurs in malfunctioning gastro-enterostomies, as not only would food be shut off from entering the intestine but the bile would be lost through regurgitation into the stomach. In such a case with high jejunal obstruction, recently observed, the obstruction was complete for eight days but plasma coagulation tests for K deficiency were constantly normal and no hemorrhagic tendency appeared.

A second type of case in which deficiency might occur would be a disturbance in intestinal absorption, such as might take place in severe diarrhea, ulcerative colitis, dysentery, multiple strictures, fistulas and possibly sprue. Such cases have been reported,[5] but a hemorrhagic diathesis developing under these conditions is distinctly uncommon. I have studied a number of patients of this type without yet encountering any in which K therapy seemed indicated. A case of sprue recently observed is a good example (chart 1). The patient never showed any hemorrhagic tendency or clinical benefit from vitamin K therapy, although his prothrombin time (Quick) was prolonged and was reduced by treatment. The blood and plasma coagulation times remained unaltered.

A third type of case in which deficiency might occur is that in which the liver has been damaged by cirrhosis or chronic hepatitis. Such damage would interfere with the utilization of the vitamin and may in certain instances lead to uncontrollable hemorrhage.[6] This

From the Department of Medicine, Stanford University Medical School.

Read before the Section on Gastro-Enterology and Proctology at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

1. Snell, Albert M., and Butt, Hugh R.: Supplementary Report on Vitamin K, J. A. M. A. **113:** 2056 (Dec. 2) 1939.

2. Snell, A. M.: Symposium on Hemorrhagic Diathesis in Cases of Jaundice: Relation to Vitamin Deficiency; Preliminary Report, Proc. Staff Meet., Mayo Clin. **13:** 65 (Feb. 2) 1938; Vitamin K: Its Properties, Distribution and Clinical Importance, J. A. M. A. **112:** 1457 (April 15) 1939. Butt, Snell and Osterberg.[6] Clark, Dixon, Butt and Snell.[5]

3. Wardell, W. W., Jr., and Du Pont, Guerry III: Effect of Vitamin K on the Clotting Time of the Prothrombin and the Blood, J. A. M. A. **112:** 2259-2263 (June 3) 1939. Dam, Henrik; Tage-Hansen, E.; and Plum, P.: Vitamin K Lack in Normal and Sick Infants, Lancet **2:** 1157-1161 (Dec. 2) 1939.

4. Kark, Robert, and Lozner, E. L.: Nutritional Deficiency of Vitamin K in Man, Lancet **2:** 1162 (Dec. 2) 1939.

5. Clark, R. L., Jr.; Dixon, C. F.; Butt, H. R., and Snell, A. M.: Deficiency of Prothrombin Associated with Various Intestinal Disorders: Its Treatment with the Antihemorrhagic Vitamin (Vitamin K), Proc. Staff Meet., Mayo Clin. **14:** 407-416 (June 28) 1939.

6. Butt, H. R.; Snell, A. M., and Osterberg, A. E.: Further Observations on the Use of Vitamin K in the Prevention and Control of the Hemorrhagic Diathesis in Cases of Jaundice, Proc. Staff Meet., Mayo Clin. **13:** 753 (Nov. 30) 1938. Pohle, F. J., and Stewart, J. K.: A Study of the Quick Method for the Quantitative Determination of Prothrombin with Suggested Modifications, Am. J. M. Sc. **198:** 622 (Nov.) 1939.

situation must be relatively uncommon, as I have encountered it only once in a series of fifty-two cases showing evidence of hepatitis and biliary tract disease. This incidence is similar to that reported by Quick [7] in 1938. In those unusual instances when free bleeding occurs basically as the result of disturbed liver function

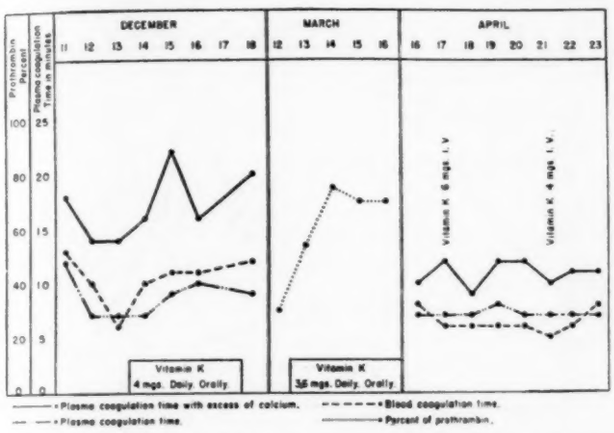

Chart 1.—Effect of vitamin K therapy in a case of nontropical sprue without any bleeding tendency. Prothrombin percentage (Quick) increased but clinical condition and blood and plasma coagulation times unaltered.

it seems unlikely that the administration of vitamin K would be effective even by the parenteral route. Such a lack of effectiveness has already been reported.[8]

A fourth type of patient in which mild K deficiency may be present and in whom it would be important to administer the vitamin is the expectant mother. A series of fifteen cases of pregnant women has already been reported [9] who have been treated with vitamin K before delivery; and it is implied that their offspring are less likely to bleed after birth when the mothers are so prepared. This work needs further confirmation.

CONDITIONS IN WHICH VITAMIN K DEFICIENCY MAY OCCUR AND THERAPY MAY BE BENEFICIAL BUT WHICH HAVE BEEN INSUFFICIENTLY STUDIED

A number of interesting clinical problems has been encountered which may be grouped under conditions in which vitamin K deficiency may occur and in which treatment may be beneficial but which have been insufficiently studied. The first concerns those cases in which deficient absorption of fat may occur which might interfere with the transportation of the vitamin through the intestinal wall. This might take place on a fat deficiency diet or might be due to disturbances in fat metabolism such as occur in cases of sprue and celiac disease and occasionally in pancreatic disorders. Also the proper absorption of fat and the vitamin might be interfered with in cases of biliary tract disease without common duct obstruction, as has been pointed out by Smith,[10] and a case of gallbladder disease has recently been reported in which such a mechanism could have been responsible for the prolonged plasma coagulation times which were encountered.[11] As certain forms of synthetic vitamin K are water soluble, their absorption would not be affected by a disturbance in fat metabolism, but it has not yet been shown that they naturally occur in a human diet.

A second group of cases which has received no attention in the literature to date is that which includes nephritis, hypertension and uremia, particularly when the late but not uncommon tendency to skin and mucous membrane hemorrhages is present. Three such cases have recently been encountered in which bleeding ceased coincident with vitamin K therapy. The effect of the treatment in one of these cases is shown in chart 2. This patient clinically showed purpura and epistaxis, and plasma coagulation time tests were slightly above normal. Bleeding ceased coincident with parenteral vitamin K therapy and the coagulation times were reduced to less than a normal average. It must be recognized that these results in this small group of cases may be purely coincidence, but they indicate that this type of problem deserves further study.

A most interesting problem is the possibility of reducing the blood and plasma coagulation times of a presumably normal person to a minimum of one or two minutes by the administration of vitamin K orally or parenterally. Six individuals without evidence of any organic disease have recently been studied from this point of view. In four of these the coagulation times of the blood and plasma were significantly reduced. The observations on one young woman with a mild psychoneurosis are shown in chart 3. She received vitamin K by mouth and a reduction in the rate of blood and plasma coagulation took place. Here again, as in the group of patients with renal disorders, the series is altogether too small from which to draw any definite conclusions, but it serves to stimulate further interest in apparently normal patients who may have subclinical K hypovitaminosis.

The observation that patients with definite vitamin K deficiency when successfully treated may show a reduction in their plasma coagulation time to less than the normal average when on adequate therapy and the possibility that the blood and plasma coagulation times

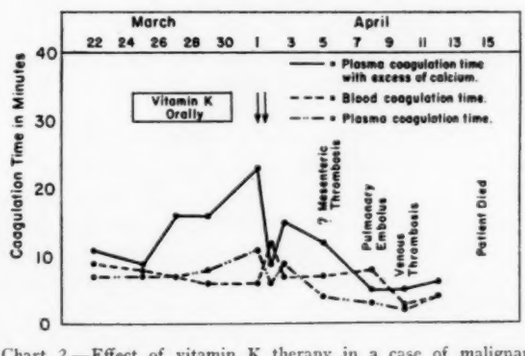

Chart 2.—Effect of vitamin K therapy in a case of malignant hypertension and uremia with purpura and epistaxis. Bleeding ceased and blood and plasma coagulation times reduced. Venous thrombosis developed. Arrows indicate single intramuscular injection of 2 mg. of vitamin K.

of normal patients may be reduced by similar treatment suggest the desirability of studying the effect of administering vitamin K preoperatively to patients in whom postoperative bleeding is to be avoided. Theoretically at least an improvement in the coaguability

7. Quick, A. J.: The Nature of the Bleeding in Jaundice, J. A. M. A. **110:** 1658 (May 14) 1938.

8. Andrus, W. DeW., and Lord, J. W.: Correction of Prothrombin Deficiencies, J. A. M. A. **114:** 1336 (April 6) 1940. Aggeler, P. M.; Lucia, S. P., and Goldman, Leon: Effect of Synthetic Vitamin K Compounds on Prothrombin Concentration in Man, Proc. Soc. Exper. Biol. & Med. **43:** 689 (April) 1940. Butt, Snell and Osterberg.[6]

9. Shettles, L. B.; Delfs, Eleanor, and Hellman, L. M.: Factors Influencing Plasma Prothrombin in Newborn Infant: Antepartum and Neonatal Ingestion of Vitamin K Concentrate, Bull. Johns Hopkins Hosp. **65:** 419 (Nov.) 1939.

10. Smith, H. P., in discussion on Stewart, J. D., and Rourke, G. M.: Control of Prothrombin Deficiency in Obstructive Jaundice, J. A. M. A. **113:** 2223 (Dec. 16) 1939.

11. Cheney, Garnett: Vitamin K Deficiency in a Case of Gallbladder Disease Without Clinical Jaundice or Hepatitis, Am. J. Digest. Dis., to be published.

of the blood might lessen the tendency to postoperative bleeding, which is particularly disturbing following operations on the eye and on the prostate. This is a field which has not yet been explored.

HEMORRHAGIC CONDITIONS IN WHICH VITAMIN K HAS BEEN SHOWN TO BE INEFFECTIVE

One of the first diseases to be studied in respect to vitamin K deficiency was hemophilia. Although the blood coagulation defect in hemophilia is very similar to experimental vitamin K deficiency in fowls, it is apparently not identical and attempts to improve the blood clotting in hemophiliac patients have met with failure. Recently I have tried repeated injections of the newer synthetic vitamin K preparations without any very encouraging results. Its use in various types of purpura whether primary and thrombocytopenic or secondary to aplastic and myelophthysic anemia or to leukemias and sepsis has proved unavailing. Such an instance is illustrated in chart 4. The patient had aplastic anemia with an almost complete absence of platelets from the blood, and skin and mucous membrane bleeding. Oral and intravenous vitamin K therapy were ineffective. Anaphylactic purpura is likewise not benefited by vitamin K therapy. This lack of success was to be expected, as these purpuric conditions are not associated with disturbances in the soluble globulin of the blood. The use of vitamin K to control blood loss from the nose, esophageal varices, gastric and duodenal ulcers, the colon, hemorrhoids and the uterus has been without proved success to date.

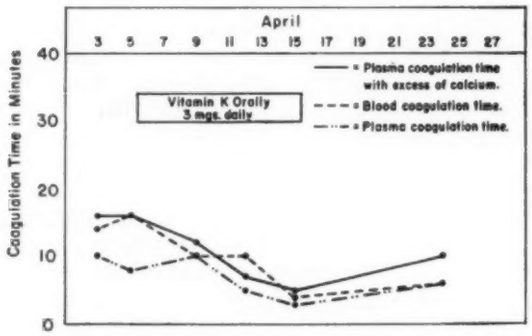

Chart 3.—Effect of vitamin K therapy on the normal coagulation times of the blood and plasma of a psychoneurotic patient on an adequate diet. Pronounced reduction occurred on the sixth day.

TESTS FOR VITAMIN K DEFICIENCY

The simplest and most certain evidence of vitamin K deficiency is the presence of hemorrhage in a patient with intense jaundice of the obstructive type and in the newborn infant. While laboratory tests are of confirmatory value, such clinical manifestations are a definite indication for immediate vitamin K therapy.

Tests of so-called prothrombin time as devised by Quick [12] and by Ziffren and his co-workers [13] have been widely used and show a reduction in the thermolabile globulin of the blood which is associated with vitamin K deficiency. An increase in these globulins occurs coincident with vitamin K therapy. They represent an indirect test for the deficiency and have proved of inestimable value in stimulating interest in the relationship of the hemorrhagic disorders of liver disease due to a lack of vitamin K. However, they present certain drawbacks which have tended to limit their usefulness. A technical disadvantage is that an unstable tissue extract must be used for the test and

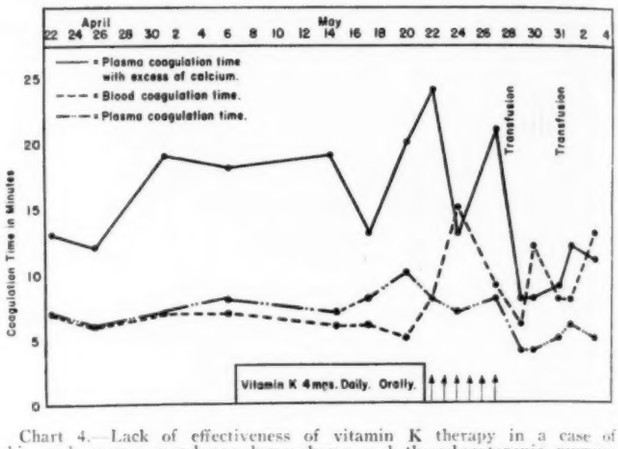

Chart 4.—Lack of effectiveness of vitamin K therapy in a case of skin and mucous membrane hemorrhages and thrombocytopenic purpura due to aplastic anemia. The bleeding was not controlled and the blood and plasma coagulation times were not reduced. Each arrow indicates an intravenous injection of 2 mg. of vitamin K.

such an extract is not readily available except in large medical centers where trained technicians are constantly performing the tests. A second drawback is the fact that the reduction in so-called prothrombin may indicate a deficiency of vitamin K but is not necessarily indicative of a hemorrhagic tendency. If the little known substances in the blood which tend to retard blood coagulation are also diminished in proportion to those which tend to accelerate coagulation, and there is no disturbance of the balance between the two,

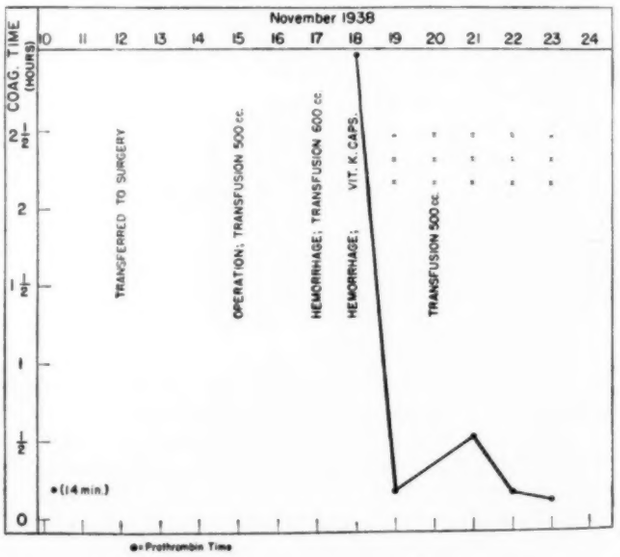

Chart 5.—Dramatic effect of vitamin K therapy in surgical case of obstructive jaundice with massive hemorrhage. Bleeding ceased and the plasma coagulation time was rapidly reduced.

the patient is no more likely to bleed than if the blood contained larger amounts of both these substances. Theoretically at least there is a third drawback in that vascular thrombosis may be produced in a patient with a diminished amount of clot promoting substances but with a normal ratio with the anticoagulation substances. Raising "the prothrombin level" under such conditions,

12. Quick, A. J.; Stanley-Brown, Margaret, and Bancroft, F. W.: A Study of the Coagulation Defect in Hemophilia and in Jaundice, Am. J. M. Sc. **190**: 501-511 (Oct.) 1935.

13. Ziffren, S. E.; Owen, C. A.; Hoffman, G. R., and Smith, H. P.: Control of Vitamin K Therapy: Compensatory Mechanisms at Low Prothrombin Levels, Proc. Soc. Exper. Biol. & Med. **40**: 595-597 (April) 1939.

which are often present in cirrhosis of the liver, might so reduce the blood and plasma coagulation times as to precipitate intravascular clotting. Three patients with extensive venous thromboses have been studied in whom these coagulation times were unusually short. One of these was the patient with hypertension and uremia (chart 2). It is, of course, possible that the thromboses in this patient were coincidental, but it must be noted that they occurred parallel with the shortening of the coagulation times.

The plasma coagulation time which is a modification of Howell's prothrombin time[14] has shown certain advantages. It has been employed in following experimental vitamin K deficiency in chicks and has proved satisfactory in the research laboratory.[14] It is a simple test, requiring but two standard chemical solutions and no unstable tissue extracts. It does not indicate a diminution of thermolabile globulin substance but a loss of balance between the clot retarding substances and the clot promoting substances, which is the real basis for the hemorrhagic defect. It may indicate a tendency toward vascular thrombosis which has already been noted. The test is not affected by platelet deficiency as ordinarily encountered in thrombocytopenic purpura. Normal coagulation times for this test are from two to eight minutes when an optimum amount of calcium is added and from three to fifteen when an excess of calcium is used.

A "serum volume test"[15] has been developed as a simple test to detect vitamin K deficiency. It has not proved serviceable in a small number of cases which I have studied.

THE THERAPEUTIC USE OF VITAMIN K

In those conditions in which vitamin K deficiency is associated with an absence of bile in the intestinal tract, the administration of bile salts alone to the patient may be all that is necessary as they will promote absorption of the vitamin. From 1 to 3 Gm. daily is adequate. It is useless to administer the vitamin in this type of case without the addition of bile salts unless a water soluble form is used. Vitamin K may be administered in a number of ways. Certain foods, notably green vegetables such as cabbage and spinach, are an excellent source, and canned mixed greens may be used in the same manner. A product of proved value[16] is made of the stalks of green grasses[17] and is effective in doses of from twelve to twenty-four tablets daily or from 3 to 6 teaspoons daily.

Medicinal products are of two types. One is an extract of alfalfa and contains the fat soluble natural vitamin. The other represents a group of synthetic products which are more or less effective, the base being napthoquinone.[1]

The choice of a preparation may be important. As far as is known at present, vitamin K from natural sources has no definite advantage over the synthetic products which are of equal potency. Food sources are desirable in that they are cheap, and cerophyl is in the same category. They usually supply an excess of the vitamin when given in usual amounts but no standardization of dosage is available. The alfalfa extract has been available for some time and is highly effective but is more costly than the synthetic products, which have the advantage of being cheap, well standardized and in certain instances water soluble, which makes some of them suitable for hypodermic injection. Parenteral therapy is more desirable than oral therapy in the treatment of infants, of patients who are vomiting and of patients in whom severe hemorrhage makes rapid control desirable. While this vitamin may be quite effective by mouth in from six to twelve hours, it is more rapidly effective by injection.[14] An average therapeutic dose of natural vitamin K or of 2-methyl-1, 4-napthoquinone is from 2 to 4 mg. daily two days before and seven days after operation. Therapy must be continued indefinitely in cases in which the cause of the deficiency cannot be relieved.

The success of treatment depends on the accuracy of diagnosis as indicated both by the clinical data and by the laboratory observations. In that group of cases in which K deficiency is known to be present the results of therapy represent an outstanding achievement in recent medical research and, in certain instances of otherwise fatal hemorrhage, may prove life saving. This is well illustrated by the case shown in chart 5. Severe postoperative bleeding was occurring subsequent to an operation on the biliary tract, and the plasma coagulation time was greatly prolonged. The hemorrhage was rapidly controlled by adequate bile salt and vitamin K therapy by mouth. Its effect on prolonged prothrombin times and on the prolonged plasma coagulation times is striking and offers a useful laboratory check on the results of the medication. However, it must be borne in mind that treating a prolonged prothrombin time is not necessarily important clinically, as it may not indicate that a hemorrhagic tendency is present. Actually, a true, clearcut deficiency of vitamin K is rarely encountered.

14. Cheney, Garnett: The Plasma Coagulation Time as a Simple Test for Vitamin K Deficiency, Am. J. M. Sc., to be published.
15. Boyce, F. F., and McFetridge, E. M.: Serum Volume Test for Hemorrhagic Diathesis in Jaundice: Further Observations, New Orleans M. & S. J. **91**: 357 (Jan.) 1939.
16. Cerophyl manufactured by the Cerophyl Laboratories, Kansas City, Mo.
17. Rhoads, J. E.: The Relation of Vitamin K to the Hemorrhagic Tendency in Obstructive Jaundice with a Report on Cerophyl as a Source of Vitamin K, Surgery **5**: 794 (May) 1939.

ABSTRACT OF DISCUSSION

ON PAPERS OF DRS. BEAN AND SPIES AND DR. CHENEY

DR. THOMAS T. MACKIE, New York: I agree with Dr. Bean and Dr. Spies with one possible reservation—the implication that the deficiency syndromes occurring in diarrheal states are commonly due to increased loss resulting from intestinal hypermotility. In my experience the rate of forward progress of the barium sulfate-water meal is rarely increased above normal and is frequently slower than normal. The roentgenologic changes demonstrable in the small intestine in deficiency disease have been shown to be associated with delayed absorption of substances such as dextrose and potassium iodide. It is probable that they contribute to progressing deficiency. As the authors have pointed out, it is important to appreciate that a major surgical procedure may precipitate an acute deficiency state. Dr. Cheney's paper is in complete conflict with the current literature on vitamin K. Data published by the Mayo Clinic group, by Quick, by Smith and by other leading authorities on the subject show conclusively that the coagulation time is not a measurement of the vitamin K status. In the presence of a normal coagulation time prothrombin deficiency may already be in the danger zone to such a degree that bleeding may occur and the patient actually die from hemorrhage before the coagulation test demonstrates any deficiency whatever. Determination of the prothrombin time or quantitative estimation of prothrombin constitutes the only direct measurement of vitamin K deficiency available at the present time. It has been amply shown that the function of vitamin K is the maintenance and activation of prothrombin, probably through the action of normal liver. Normal blood of man and animals has a prothrombin content far in excess of the amount needed for normal blood coagulation. This natural "hyperprothrombinemia" appears to be physiologic. No data are available to show that vitamin K

may induce an abnormally high prothrombin level. If the orthodox theory of blood coagulation is correct, intravascular clotting cannot be produced by vitamin K, and hyperprothrombinemia has not been observed in thrombosis. Furthermore the blood clotting test which Dr. Cheney has used is not a measure of a pathologic condition even in the presence of thrombosis.

DR. DONALD T. CHAMBERLIN, Boston: My experience with avitaminosis has been in the dietary management of postoperative cases, particularly those following subtotal gastric resection. Following resection, one finds the beefy, rough, sharp-pointed tongue, usually heavily furred, dry mouth and skin, sometimes diarrhea when feeding is begun on the fourth or fifth postoperative day, and usually irritability and occasionally neuritides, though the latter are rare. Formerly these symptoms were thought to be the result of the procedures or of dehydration or both; however, the early improvement resulting from the use of parenteral vitamin B in the form of crude liver extract, or injectable vitamin B complex, makes the diagnosis of vitamin deficiency in these cases certain. My custom has been to start liver injections or vitamin B complex injections, or both, on the second or third day. I have found that by the eighth or tenth day the clinical signs of vitamin deficiency have largely disappeared, the tongue is flat, clean, pink and moist, the eye is bright and the skin warm and moist. I have not noticed any increase in the healing rate of the wound. The loss of vitamins through the digestive tract in diarrheal states is undoubtedly large but difficult to measure and to evaluate. If the diarrhea is the result of a general change in the entire digestive tract there is a greater loss of the fat-soluble vitamins as well as the water-soluble ones than when the lesion, such as ulcerative colitis, involves only the colon, and the absorptive powers of the small intestine are intact. In general, patients with diarrhea who receive additional vitamins improve in appetite and physical well being; however, except in the case of diarrhea as a symptom of primary vitamin deficiency, other measures must be used to check the diarrhea. In my experience diarrhea as a symptom of primary vitamin deficiency has been rare. The points requiring emphasis in the use of Vitamin K are these: 1. In severe liver damage and in such conditions in which fat metabolism is disturbed, as sprue, the prothrombin level may not be appreciably raised or, if raised, may not stay up. 2. It is of the utmost importance to raise the prothrombin level as high as possible and not be satisfied with levels from 70 to 85 per cent of normal, before contemplated operative procedures are carried out. 3. If the level cannot be raised, bleeding must be expected postoperatively.

DR. MANDRED W. COMFORT, Rochester, Minn.: May I join Dr. Mackie in emphasizing the fact that hypoprothrombinemia occurs in four major conditions: (1) inadequate intake of food containing vitamin K, (2) impairment of absorption referable to lack of bile in the intestine, (3) impairment of absorption caused by deficient absorptive surfaces and (4) hepatic insufficiency preventing the utilization of vitamin K. Hypoprothrombinemia, as well as the resulting tendency toward hemorrhage, has been encountered in a variety of diseases or conditions, including obstructive jaundice, sprue, intestinal obstruction, short-circuiting operations such as gastro-ileostomy which reduce the absorptive surfaces of the small bowel, and hepatic diseases of various types. Hypoprothrombinemia plus the associated hemorrhagic tendency has responded satisfactorily to preparations of vitamin K derived both from alfalfa and from fish meal; it has also responded to the synthetic preparations, which are administered orally and parenterally. Toxic reactions have not occurred. The decrease in the prothrombin clotting time (the laboratory measurement of the degree of hypoprothrombinemia present), as well as the cessation of bleeding, occurs within a few hours. The preparations of vitamin K thus far used have been ineffectual in reducing the prothrombin clotting time and in stopping hemorrhage only in cases of advanced disease of the liver, chiefly cirrhosis. The failures in the early use of vitamin K have largely been eliminated by the prescription of adequate dosage in prophylactic and curative therapy and by the use of preparations to be administered intravenously.

DR. JOHN L. KANTOR, New York: There are two points I should like to make. One is a plea to Dr. Bean and his collaborators to simplify the nomenclature of the dosage of the vitamins. It is confusing to have two or three different kinds of nomenclature, international units, Sherman units and micrograms, to carry in mind. Now that we have crystalline products available, wouldn't it be a great help to all of us to have the dosage recorded in milligrams? It would simplify administration and make for clarity in the use of these important substances. My second point is directed toward Dr. Cheney. He has apparently not yet encountered a hemorrhage in the case of deficient intestinal absorption. This possibility was already stressed by Dr. Mackie. I should like to call attention to a brief discussion of hemorrhage in the sprue type of defective intestinal absorption published in the May issue of the *Archives of Internal Medicine*. When bleeding does occur it may be very serious indeed. At present it is a great comfort to know that the administration of vitamin K will control the symptoms, not only the massive hemorrhages in the intestinal tract but also those in the skin. A word of caution: If the vitamin K is administered by mouth it is usually in a fat medium which cannot be absorbed; it is therefore important to give it in a water-soluble medium, either by mouth or parenterally, so that it can be absorbed in these cases of deficient fat utilization.

DR. WILLIAM BENNETT BEAN, Cincinnati: In answer to Dr. Mackie's statements about intestinal motility in diarrheal states, in many of our cases there was advanced organic disease of the colon or ileum as seen at postmortem. We have given dyes or glass beads, which occasionally appeared in the stool within an hour but were usually apparent between four and six hours contrary to his experience when using barium. In these cases we found particles of undigested food, so this rapidity of transit through the alimentary canal was a factor leading to vitamin deficiency. Whether that is generally so in cases of uncomplicated diarrheas due to deficiency disease I don't know, but in cases of definite organic disease it was a factor. The indications for vitamin B_6 are difficult to predict with certainty. The patients whom we have successfully treated were endemic pellagrins or beriberi patients who had been given large doses of nicotinic acid, thiamine hydrochloride and riboflavin and who, following each of these materials, had an increased feeling of well being and relief of specific symptoms and yet were still not completely well. Their complaints were ataxia, difficulty in walking, muscular weakness, nystagmus, pains in the epigastrium and inability to work. Their diets during the time were grossly deficient. When large doses of vitamin B_6 were given, some of the patients got dramatic response but some were not specifically helped. It was impossible to predict which would be helped. It was definite that certain ones were able to get up and walk and had a definite feeling of well being, lost the nystagmus and ataxia and were able to perform muscular movements previously impossible. As far as operations go, when dextrose is given in large amounts to any individual in a borderline state of nutrition it is very likely to precipitate a crisis of deficiency disease, and one method to control experimental therapy is to put the patient to bed and give nothing but dextrose and water by mouth. This may be a factor in several postoperative complications. We have a feeling that there will come a time when physicians will cover such administrations of dextrose with B complex vitamins, as is now done with insulin. Dr. Kantor's question regarding dosage is exceedingly important. It is illogical to talk in terms of units derived from assays of impure materials when we have pure chemical substances which can be weighed. Calculations should be made in terms of grams, milligrams and micrograms.

DR. GARNETT CHENEY, San Francisco: I can best answer most of the points that Dr. Mackie raised that were contrary to what I presented by saying this: First, he seems to be about where we were two years ago when we relied on prothrombin determinations alone for our study of vitamin K deficiencies. Second, I can't help but believe that Dr. Mackie has not studied this disease in clinics for a long period, as we have. That goes over a five year period. As long as he relies on so-called quantitative prothrombin—and nobody knows what that is—determinations on which to base his whole classification of K deficiency, I believe we are not talking on the same level; consequently I can't go into that any further with the time allotted to me. I am familiar with bleeding in sprue. I simply stated that we had not seen it, and I cannot help but feel that a laboratory test such as the prothrombin time, which is notoriously unreliable even in the hands of skilled workers, cannot be accepted

as the final word in determining vitamin K deficiency; and I am familiar with the fact that a number of others agree with that. I was rather hasty with regard to dosage and therapy. It has been our habit to give 2 mg. a day or more. We have given it parenterally. The slides I went over showed the rapid response in vitamin K deficiency and obstructive jaundice to therapy. The patient with gallbladder disease received three injections in twenty-four hours with a reduction in time within a matter of hours which showed clearly on the chart, but I did not have time to emphasize that point. I certainly didn't mean to give the impression that vitamin K was not highly efficacious in the type of case in which it should be given. I think its use represents one of the most important recent advances in medical treatment and I am sorry if I gave any impression to the contrary. I did want to emphasize that I think its use must be limited to definite groups of cases and, as long as we treat and just use a laboratory test such as prothrombin time, we may treat some patients unnecessarily.

THE INFLUENCE OF THE LIVER ON THE UTILIZATION OF VITAMIN K

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AND
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It is now well established that proper administration of vitamin K and related compounds will in most instances prevent or control hemorrhage resulting from a deficiency of prothrombin. It has been reported also that administration of these substances is less effective when the prothrombin deficiency is associated with extensive hepatic damage (Smith, Warner and Brinkhous,[1] Warner,[2] Butt, Snell and Osterberg,[3] Stewart and Rourke,[4] Pohle and Stewart[5]).

The present study was undertaken to determine any possible correlation between the condition of the liver, the occurrence of a deficiency of prothrombin and the subsequent utilization of vitamin K. Hepatic damage was produced by uniform exposure of rats to a known concentration of carbon tetrachloride. The susceptibility of the liver of these animals to carbon tetrachloride was varied by the use of different dietary levels of carbohydrate, protein and fat. Crude concentrates of alfalfa and 2-methyl-1, 4-naphthoquinone were administered to some of these animals and in all instances failed to increase the level of prothrombin in the circulating blood. A detailed study was made also of the possible causes of these failures. The only common factor found was that extensive hepatic injury was associated with depletion of the level of prothrombin and also with failure of response to vitamin K.

From the Division of Experimental Medicine, the Mayo Foundation (Dr. Bollman), and the Division of Medicine, the Mayo Clinic (Dr. Butt and Dr. Snell).

Read before the Section on Pathology and Physiology at the Ninety-First Annual Session of the American Medical Association, New York, June 14, 1940.

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2. Warner, E. D., in discussion on Butt, H. R.; Snell, A. M., and Osterberg, A. E.: Oral and Intramuscular Administration of Vitamin K in Hemorrhagic Diathesis of Obstructive Jaundice, abstr. J. A. M. A. **112:** 879-880 (March 4) 1939.

3. Butt, H. R.; Snell, A. M., and Osterberg, A. E.: The Preoperative and Postoperative Administration of Vitamin K to Patients Having Jaundice, J. A. M. A. **113:** 383-389 (July 29) 1939.

4. Stewart, J. D., and Rourke, G. M.: Control of Prothrombin Deficiency in Obstructive Jaundice by Use of Vitamin K, J. A. M. A. **113:** 2223-2227 (Dec. 16) 1939.

5. Pohle, F. J., and Stewart, J. K.: Observations on the Plasma Prothrombin and the Effects of Vitamin K in Patients with Liver or Biliary Tract Disease, J. Clin. Investigation **19:** 365-372 (March) 1940.

EXPERIMENTAL PROCEDURE

Male white rats (Wistar strain) weighing approximately 200 Gm. each were fed a basic diet which consisted of 44 parts of lean meat, 44 parts of cracker meal, 8 parts of lard and 4 parts of salt mixture and vitamin supplement. Normal rats take 20 Gm. of this diet daily. The rats used in this experiment were kept in individual cages and the uneaten portion of the food was reweighed each day. The mixed diet was fed in 20 Gm. amounts; carbohydrate diet consisted of 10 Gm. of the mixed diet and 7 Gm. of cracker meal; the protein diet was 10 Gm. of the mixed diet and 10 Gm. of lean meat; the fat diet was 10 Gm. of the mixed diet and 3 Gm. of lard. The amounts thus fed were isocaloric. All animals were given the experimental diet for from five to seven days prior to exposure to carbon tetrachloride.

The rats were placed in a closed chamber and exposed to carbon tetrachloride vapor for thirty minutes three times each week as long as the animals survived. The concentration of carbon tetrachloride vapor was uniformly maintained by vaporizing 1 cc. of carbon tetrachloride in 10 liters of air passed through the chamber each minute. The rats were semiconscious at the end of each exposure but recovered rapidly when returned to their cages in air.

EXPERIMENTAL RESULTS

All of the rats that died as a result of the repeated administration of carbon tetrachloride were found to have massive accumulation of blood in the gastrointestinal tract. Many animals gave evidence of intestinal bleeding several days before death. Tarry stools were noted and in many animals signs of anemia were also present. Blood taken at this time usually showed delayed clotting time and in all cases the prothrombin level was found to be less than 30 per cent of the normal value (Quick[6]). Other animals taken before signs of hemorrhage were evident usually showed normal clotting time of the blood but some reduction of the prothrombin content. No definite time relationship was found between the duration of the carbon tetrachloride regimen and the time of reduction of the prothrombin. Usually the changes were not present until the third week but there were numerous exceptions both earlier and later.

The addition of vitamin K concentrates (from 1,000 to 5,000 Dann units daily) to the diet had no influence on the survival time of the rats that received carbon tetrachloride, nor did the further addition of bile salts to the diet show any influence on the occurrence of hemorrhage. Intramuscular injections of vitamin K concentrates, both in water and in oil, were likewise ineffective, as was the oral and subcutaneous administration of 2 mg. daily of 2-methyl-1, 4-naphthoquinone. Likewise the administration of vitamin K proved ineffective in increasing the prothrombin content of the blood of rats found deficient in prothrombin following continued administration of carbon tetrachloride. When administration of carbon tetrachloride was discontinued to animals found deficient in prothrombin, normal amounts of prothrombin were found in from seven to ten days. No definite acceleration of prothrombin formation was found in similar animals which were given large amounts of vitamin K.

Although gross hemorrhage into the intestine was a prominent feature in the condition found at necropsy,

6. Quick, A. J.: The Clinical Application of the Hippuric Acid and the Prothrombin Tests, Am. J. Clin. Path. **10:** 222-233 (March) 1940.

microscopic examination of sections from the intestine did not show any evidence of bleeding from large vessels. Petechial hemorrhages were observed in the capillaries of the mucosa in all animals. In many these were confined to the capillaries of the villi of the jejunum, but in others bleeding from almost all of the mucosal capillaries was observed. In a few animals petechial hemorrhages were also observed throughout the entire gastrointestinal tract including the stomach and colon. The greatest changes were always found in the jejunal portion, however. A typical picture of capillary hemorrhage in a jejunal villus is shown in figure 1. Capillary hemorrhage was also frequently found in other organs to a lesser degree than in the intestine. Listed in order of the magnitude of the bleeding observed microscopically, these organs are the liver, kidney, lung, adrenal and pancreas. A few petechial hemorrhages were found occasionally in the heart and skeletal muscle. Because this pathologic change seemed similar to that reported by Griffith and

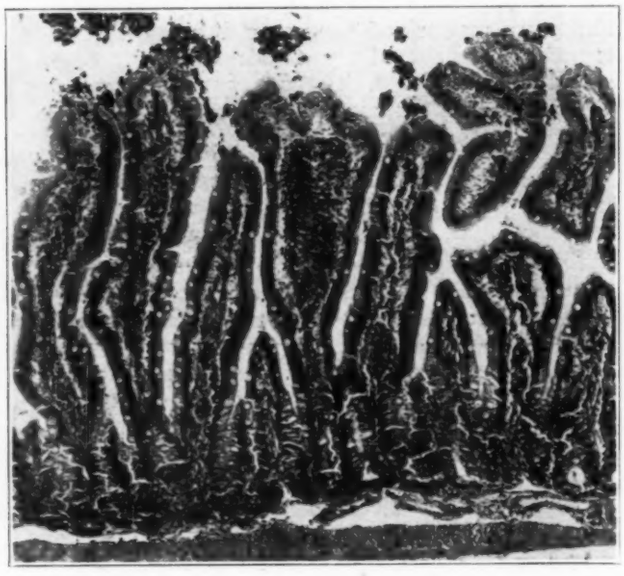

Fig. 1.—Typical capillary hemorrhage in a jejunal villus of a rat that died after thirty-four days of the carbon tetrachloride regimen; × 100.

Wade [7] in young rats on a choline-deficient diet, we added 20 mg. of choline daily to the diet of a series of rats receiving carbon tetrachloride. This addition, however, proved ineffective in preventing or delaying the occurrence of hemorrhage in our rats.

The only organ that showed cellular degeneration other than that immediately associated with hemorrhage at the time of death from bleeding after the carbon tetrachloride regimen was the liver. Extensive necrosis was present in this organ and it was usually difficult to find any liver cells which did not show evidence of degeneration. Usually only a few cells remained that could be recognized as hepatic cells. In the animals that survived the longer times there were accumulations of connective tissue and distortion of the architecture of the liver, which indicated that some regeneration of the previously damaged liver had occurred but that the new liver cells were later killed by subsequent carbon tetrachloride. In the animals studied at the time of death no differences in the extent of degeneration of the liver could be observed which could be ascribed to the different diets taken by the animals. The survival time and other essential data concerning the rats which died from hemorrhage during the carbon tetrachloride regimen are summarized in table 1. It should be noted that the rats that received the carbohydrate diet survived about 50 per cent longer than the rats on the other diets, while those that received the fat diet died about 12 per cent earlier than those on the mixed or the protein diet.

TABLE 1.—*Carbon Tetrachloride Regimen: Death from Hemorrhage*

Diet	Number of Rats	Lived Days, Average	Loss in Body Weight, Gm.	Per Cent of Diet Taken	Rats with More Than Average Food Lived Days
Mixed	58	33	8	70	36
Carbohydrate	39	49	6	81	51
Protein	58	34	24	82	32
Fat	67	29	21	70	28

Microscopic examination of sections of liver taken from rats at various times during the carbon tetrachloride regimen, but before bleeding had occurred, showed some evidence of the protective effects of the diet. Because of the severity of the regimen all the livers were extensively damaged after the first few days and there were no great outstanding differences in appearance with the different diets used. At the same time intervals the greatest amount of necrosis was usually found in the livers of the fat-fed animals and the least in the carbohydrate-fed animals. In some instances the difference was very marked but in others no choice could be made. However, when a difference was present in comparable animals it was always in favor of the carbohydrate-fed animals showing the least amount of necrosis. Regenerative changes in the liver as indicated by the number and size of the round islands of newly formed liver cells were most marked in the meat-fed animals. In many instances these islands of regenerated liver cells did not show as extensive degenerative changes as were found in the other parts of the same liver or were present in the liver of comparable rats on other diets. It should also be noted that no correlation could be established between the histologic appearance of the liver and the prothrombin content of the blood except for the fact that there was extensive hepatic degeneration in all the animals studied.

TABLE 2.—*Carbon Tetrachloride Regimen: Chemical Changes*

			Analysis of Hepatic Tissue					
Rat	Coagulation Time, Min.	Prothrombin (Quick), per Cent	Glycogen, per Cent	Total Lipoids, per Cent	Phospholipids, per Cent	Days of Carbon Tetrachloride Regimen	Diet	Change in Weight, Gm.
a	5	15	0.20	8.7	2.1	22	Mixed	— 8
b	3	90	0.16	7.6	2.8	22	Carbohydrate	— 5
c	3	40	0.19	5.7	2.4	22	Protein	—15
d	3	35	0.18	7.6	2.3	22	Fat	—40
e	3	30	0.37	7.3	2.5	39	Mixed	+18
f	6	30	0.18	6.1	2.2	39	Carbohydrate	+14
g	3	80	0.20	6.7	2.4	39	Protein	—24
h	6	20	0.15	11.3	2.1	39	Fat	+ 3

Chemical analysis of the livers taken at different times during the regimen likewise failed to show any correlation between the diet used and the prothrombin deficiency. In all animals the carbon tetrachloride pro-

7. Griffith, W. H., and Wade, N. J.: Choline Metabolism: I. The Occurrence and Prevention of Hemorrhagic Degeneration in Young Rats on a Low Choline Diet, J. Biol. Chem. **131**: 567-577 (Dec.) 1939.

duced a marked lowering of the glycogen content of the liver, approximately a 90 per cent decrease. No marked changes were produced in the lipoid content of the liver; the phospholipids and the choline-containing phospholipids were within normal limits but the neutral fat content of the liver tended to increase with time on the regimen and was usually but not always greater in the fat-fed animals. These changes are indicated in table 2. Figure 2 shows the histologic changes of these same livers.

Because of the extensive necrosis of the liver in the animals that showed a prothrombin deficiency and an increased coagulation time, it was considered that an excess of heparin might be present in the blood.[8] Neutralization experiments with protamine added to normal blood and to the prothrombin-deficient blood did not nullify the difference in coagulation time between the normal and the experimental blood. The intravenous injection of as much as 100 mg. of protamine likewise failed to alter the coagulation time or the prothrombin time of blood drawn at subsequent intervals.

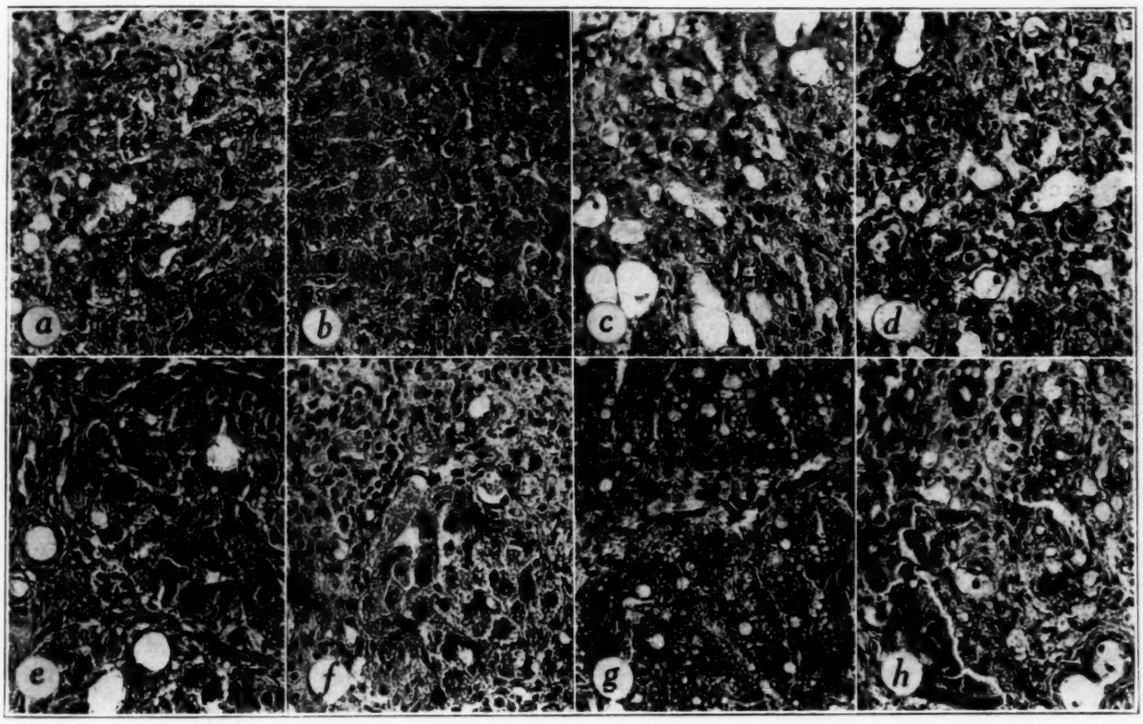

Fig. 2.—Sections of the livers from rats of table 2. All sections show marked degenerative changes. These sections which are representative of the usual appearances show that less degenerative changes occur in the carbohydrate-fed animals. *a* to *d* inclusive, received carbon tetrachloride twenty-two days each; *e* to *h* inclusive, received carbon tetrachloride thirty-nine days each. Examination of sections at a lower magnification than this indicates a greater number of newly formed islands of liver cells in the animals securing the meat diet; × 200.

CLINICAL RESULTS

The following two cases represent instances of severe hepatic damage associated with a deficiency of prothrombin. The coagulation defect in these cases likewise failed to respond either to large doses of crude concentrates of alfalfa or to synthetic compounds exhibiting marked antihemorrhagic activity.

CASE 1 (fig. 3).—Without any previous significant history except for chronic alcoholism and the use of cinchophen, painless jaundice developed. On examination the concentration of hemoglobin was found to be 13.3 Gm. per hundred cubic centimeters of blood, with 6,800 leukocytes per cubic millimeter of blood. Urinalysis showed a trace of bile, red blood cells graded 3 on a basis of 1 to 4, and an occasional pus cell. The serum bilirubin was 4.7 mg. per hundred cubic centimeters with a direct van den Bergh reaction. Roentgenograms of the gallbladder showed a nonfunctioning organ with stones. The flocculation reaction was positive. Roentgenograms of the chest were negative and roentgenograms of the spine revealed only hypertrophic changes in the lumbosacral joints. The serum protein was 6.5 Gm. per hundred cubic centimeters and the bromsulphalein test of liver function revealed dye retention grade 3. The blood cholesterol was 187 mg. and the cholesterol esters were 93 mg. per hundred cubic centimeters of plasma.

The patient became progressively worse in the hospital, and ascites and edema developed; there was also considerable bleeding from the mouth and the gastrointestinal tract. Death was due to hepatic insufficiency. Necropsy revealed cirrhosis of the liver with ascites.

CASE 2.—A woman aged 38 had had painless jaundice for ten months prior to admission. On examination an orange-yellow discoloration of the skin was noted. The liver and spleen were enlarged, grade 2. There was no evidence of ascites or collateral circulation. There were a few large purpuric spots on her extremities. Otherwise the results of her physical examination were essentially negative.

Urinalysis revealed albumin grade 1, granular casts, and pus grade 1 on the basis of 1 to 4. The hemoglobin was 11 Gm. per hundred cubic centimeters of blood with 4,430,000 erythrocytes and 5,200 leukocytes per cubic millimeter. Blood smears showed hypochromic macrocytosis. The serum bilirubin was 13.8 mg. per hundred cubic centimeters and the van den Bergh reaction was direct. The sedimentation rate was 117 mm. in one hour. The results of the routine flocculation test and roentgenologic examination of the chest were negative. The prothrombin time was forty-two seconds.

Soon after the patient's admission she had a nosebleed and the prothrombin time was further elevated. Following vitamin K therapy the bleeding ceased and the prothrombin time dropped a little but rose again promptly (fig. 4). It was never reduced to less than thirty-two seconds. During her last three weeks illness in the hospital ascites and edema, as well as frequent nosebleeds and purpuric spots on her thighs, developed. The serum bilirubin rose steadily during the last

8. Dam, Henrik, and Glavind, Johannes: Application of the Tissue Extract Method for the Standardization of Heparin, Skandinav. Arch. f. Physiol. **82**: 221-224, 1939.

two weeks of life. The patient maintained a good urinary output but finally lapsed into hepatic coma. This responded temporarily to the administration of oxygen, dextrose, thiamine hydrochloride and nicotinic acid. Whenever these substances were withdrawn, she lapsed again into coma. The last four days of her life she was almost constantly comatose and there was a considerable amount of bleeding from the bowel. Pneumonia of the base of the right lung developed about a week before she died. Necropsy revealed advanced cirrhosis of the liver.

COMMENT

It should be noted that in all of these experiments the procedure used produced extensive damage to the liver. The small differences noted in the histologic picture of sections of liver from the animals on different diets were due largely to the severity of the procedure. Much greater differences in hepatic damage and survival are rapidly evident when diets deficient in carbohydrate or protein are used. However, in the experiments reported here all the diets contained slightly more of these substances than is necessary for the basal metabolism of the animal and the amount of carbohydrate, protein or fat added to provide additional caloric intake for the animal's activity. Animals not exposed to carbon tetrachloride lived in normal appearing conditions when these diets were fed.

The failure of certain patients with hepatic disease to respond to vitamin K therapy with an elevation of the prothrombin content of the blood appears to be evidence of grave liver impairment. Many of these patients will be found to have suffered irreparable injury. The same failure of prothrombin response to vitamin K may be produced in animals concomitant

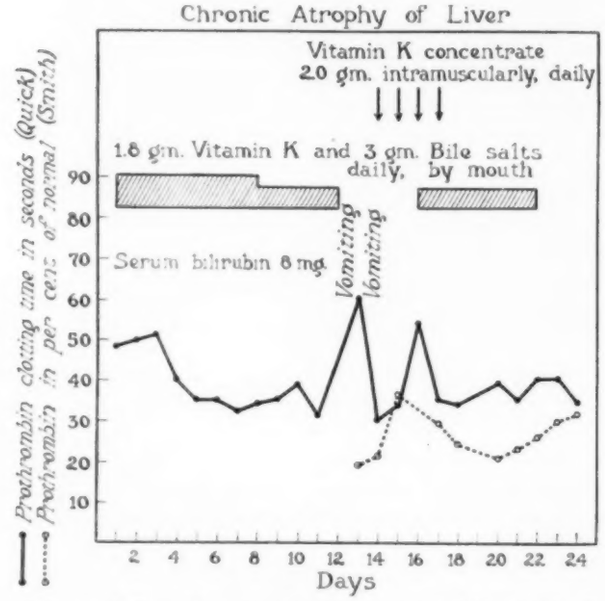
Chronic Atrophy of Liver
Vitamin K concentrate
2.0 gm. intramuscularly, daily
1.8 gm. Vitamin K and 3 gm. Bile salts daily, by mouth
Serum bilirubin 6 mg.
Vomiting
Vomiting
Prothrombin clotting time in seconds (Quick)
Prothrombin in per cent of normal (Smith)
Days

Fig. 3.—Failure of response to concentrate containing vitamin K.

with severe hepatic necrosis. It is encouraging to note that in such animals prompt recovery occurs when the hepatotoxic agent is removed and the liver repair is rapid. Even if administration of the hepatotoxic agent is continued, life may be prolonged by the use of diets rich in carbohydrates.

SUMMARY

Severe hepatic injury is invariably associated with a deficiency of prothrombin in the circulating blood. If the hepatic injury is severe enough, the administration of vitamin K is not effective in correcting this deficiency of prothrombin.

With our experimental procedure, extensive hepatic damage was produced in all animals. Livers from comparable animals that received a basic diet to which had been added carbohydrate, protein or fat showed a marked decrease in glycogen. On microscopic examina-

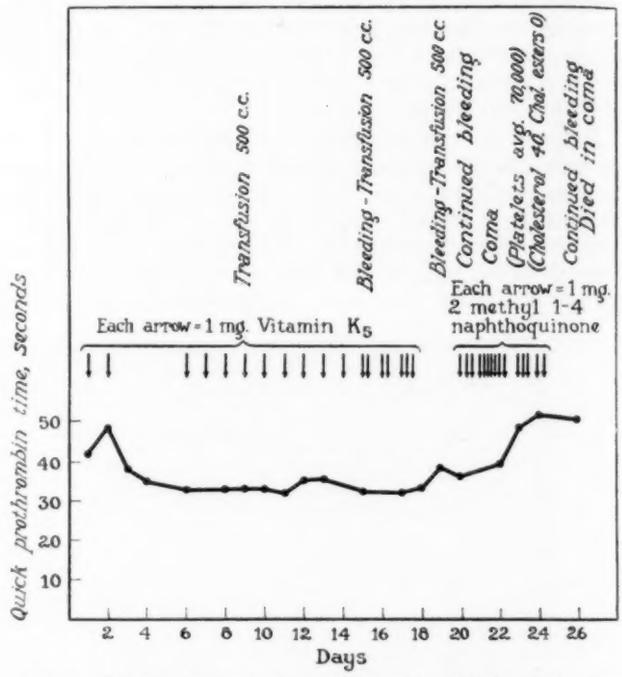

Fig. 4.—Prothrombin level of a patient with cirrhosis of the liver showing failure to respond to vitamin K (2-methyl-4-amino naphthol hydrochloride) supplied by Parke, Davis & Co.; a water-soluble compound of 2-methyl-1, 4-naphthoquinone supplied by Abbott Laboratories, North Chicago, Ill.

tion, the extent of hepatic necrosis appeared greatest with the fat diet and least with the carbohydrate diet, while regenerative changes were more marked in the protein-fed animals. These changes were small in comparison with the extensive necrosis present and no correlation could be made between the condition of the liver and the amount of prothrombin in the blood. However, the animals that received the carbohydrate diet survived without hemorrhage about 50 per cent longer than did those that received other diets.

The deficiency of prothrombin and the lack of response to vitamin K does not appear to be the result of a deficiency of choline either in the diet or in the injured liver. The heparin content of the blood and its antithrombin activity are not greatly altered by extensive hepatic damage.

The failure of vitamin K to maintain the prothrombin level of the blood and the rapid recovery to normal levels of prothrombin after discontinuation of exposure to the hepatotoxic agent indicate that the liver is of fundamental importance in the formation of prothrombin and in the metabolism of vitamin K.

ABSTRACT OF DISCUSSION

DR. STEPHEN MADDOCK, Boston: This is an important paper from both the scientific and the clinical point of view. We have noted at the Boston City Hospital that there are some patients who will not respond to vitamin K, just like the two of Dr. Snell's that Dr. Bollman quoted. When patients of this sort are discovered the prognosis is bad. In reading the original manuscript of Dr. Bollman and his co-authors I noted that the meat-fed animals showed more marked regenerative changes than those on other diets. The islands of regenerating tissue also manifested less susceptibility to subsequent exposure to carbon tetrachloride. Although this fact has been

pointed out by others (Whipple, Opie, Ravdin) the clinician still firmly believes that an almost exclusively carbohydrate diet is necessary in severe liver damage. It may be that a combination of carbohydrate with protein, such as giving plasma intravenously along with dextrose, would be more useful. The question of the mechanism of this failure of vitamin K to work is also quite important. Is it that the liver is required to do something to the vitamin K intake? Does it furnish some co-factor? Or is it possible that in addition to damaging the liver some other factors come in? I did not see anything about fibrinogen determinations, and the prothrombin times were done by the Quick method, which will be definitely affected by lowered fibrinogen. I imagine the authors determined the fibrinogen and said nothing about it. Another question which comes up is whether or not there is an increase in some anticoagulant in the blood. In the original manuscript they determined whether or not heparin was responsible for this bleeding by giving protamine intravenously to their animals. They found no change, so that heparin can be eliminated, but it is possible that there might be some other anticoagulant which could be responsible for the bleeding.

DR. JONATHAN RHOADS, Philadelphia: We have been able to induce hypoprothrombinemias in Philadelphia with carbon tetrachloride, but we have not had as refined a technic as Dr. Bollman has shown you. We have simply given the material by mouth and it works well. Some years ago, when the question of the source of fibrinogen was being studied at the Mayo Foundation, Dr. Mann made the statement that the fact that a hepatotoxic agent will produce a given change cannot be used as proof that the liver is involved in the change. We were so impressed with the logic of this view that Dr. Richard Warren and I performed total hepatectomy in a number of dogs. The prothrombin level declined progressively in these animals until they died. The fall in the prothrombin level was much more rapid than the concomitant fall in fibrinogen concentration. We have observed several patients with hypoprothrombinemia who have failed to respond to vitamin K. While such patients do not all have a bad prognosis, many of them do. Two of these patients died within thirty-six hours after the prothrombin started to rise, another a little later. Sections of the liver obtained at autopsy showed extensive fibrous changes and only scattered liver cells having a normal appearance. With regard to the effect of diet on liver injury produced by carbon tetrachloride in rats, the results obtained by Dr. Bollman were somewhat at variance with those obtained by Goldschmidt, Vars and Ravdin in 1939, who found that in protecting rats against the effects of one hour of chloroform anesthesia much the best results were obtained with a diet that was high in carbohydrate but also high in protein. I should like to ask Dr. Bollman whether any analyses were made on the meat supplement. In Dr. Ravdin's laboratory, difficulty was encountered in using a supplement of beef heart. The expected results were not forthcoming, and it was found on looking up the analysis of beef heart that it contained a substantial amount of fat and that it was necessary to use a pure protein such as casein for the protein supplement.

DR. JESSE L. BOLLMAN, Rochester, Minn.: Dr. Maddock called attention to some things I forgot. He asked about fibrinogen determination. We did determine fibrinogen in our rats. I did not say anything about these determinations because our results were extremely variable. However, in using the Quick method for prothrombin I found it to be accurate in that I can add normal blood, which contains a normal amount of fibrinogen, and also a normal amount of prothrombin to bloods of low prothrombin content. I have diluted this blood; then adding the amount of diluted blood I can determine to a matter of 1 or 2 per cent, I am sure, the actual prothrombin content by the Quick method. Dr. Rhoads brought the difference between my results and the results of Ravdin and his associates. I believe that Dr. Rhoads will agree that changes in the liver, histologic changes in the liver that I showed you, are not of outstanding difference in those different animals. It is pretty much a matter of opinion. Also, considering the fact that Dr. Ravdin's experiments were acute experiments following the administration of one dose of chloroform, and I used carbon tetrachloride repeatedly, I am not surprised that we can get from a histologic standpoint a variation of opinion. With reference to the utilization of protein, we used muscle for our protein. We also have another series in which I have used casein and another series gelatin, and there is no essential difference among the three.

EPIDEMIC CEREBROSPINAL MENINGITIS (MENINGOCOCCIC)

THE TREATMENT OF 113 PATIENTS WITH ANTIMENINGOCOCCUS SERUM, MENINGOCOCCUS ANTITOXIN AND SULFANILAMIDE

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One hundred and thirteen cases of epidemic cerebrospinal meningitis, representing for the greater part a small epidemic of the disease in Rhode Island, have been admitted to the Charles V. Chapin Hospital since February 1935. The epidemic gave us an opportunity to study the method of treatment of the "genus epidemicus" type of the disease and also to determine the relative therapeutic value of the antimeningococcus serum, the meningococcus antitoxin of Ferry and sulfanilamide.

ANTIMENINGOCOCCUS SERUM

A routine method of treatment, similar to the one which had been used successfully at the Herman Kiefer Hospital by Gordon [1] during the 1927 to 1931 epidemic in Detroit, was adopted at the beginning of the epidemic when severe and fulminating cases were encountered. This consisted of alternate lumbar and cisternal injections of antimeningococcus serum at intervals of twelve hours during the first thirty-six or forty-eight hours. After this period treatment was administered once daily, preferably by the lumbar route. The doses for intrathecal treatment were from 5 to 10 cc. less than the amount of spinal fluid removed.

TABLE 1.—*Comparison of Case Fatality Rates in Two Groups of Cases Treated with Antiserum and Antitoxin*

	No. of Cases	No. of Deaths	Fatality Rate of All Deaths	Within 48 Hours		Excluding Deaths Within 48 Hours
				Deaths	Rate	
Antiserum	43	18	41.8%	7	38.9%	30.0%
Antitoxin	33	14	42.4%	8	57.1%	24.0%
Totals	76	32	42.1%	15	46.9%	27.9%

Immediately after the initial intraspinal injection and after a satisfactory sensitivity test for horse serum, a large dose of the antiserum (from 30 to 60 cc. for infants and young children and 90 to 120 cc. for older children and adults), diluted two or three times by volume in physiologic solution of sodium chloride containing 5 or 10 per cent dextrose, was given intravenously. These doses given once or twice were ordinarily sufficient but, in very severe cases and those showing persistent septicemia, larger amounts of the antiserum were given several times, preferably during

1. Gordon, J. E.: Medical Report of the Herman Kiefer Hospital for the Five Years 1927-1931, Detroit, Department of Health, Division of Epidemiology.

the first twenty-four hours. Intrathecal treatment was continued until two consecutive negative spinal cultures were obtained.

The first eight of the 113 patients were treated entirely with antimeningococcus serum of several standard brands. Five of these died, a case fatality rate of 62.5 per cent.

ANTIMENINGOCOCCUS SERUM AND MENINGOCOCCUS ANTITOXIN

About this time (March 23, 1935) Hoyne [2] reported 296 cases of epidemic cerebrospinal meningitis from the contagious disease department of the Cook County Hospital, Chicago. Eighty-five of these were treated with the meningococcus antitoxin of Ferry [3] and the remainder, or 211 cases, with two well known standard brands of antimeningococcus serum. The fatality rate in the antitoxin-treated cases was 23.5 per cent compared with 45.9 per cent for antiserum-treated cases.

TABLE 2.—*Cases and Deaths by Ten Year Age Groups*

Age Group	Cases	Deaths	Fatality Rate
1 to 10	35	10	28.6%
11 to 20	16	10	62.5%
21 to 30	10	5	50.0%
31 to 40	9	3	33.3%
41 to 50	3	2	66.6%
51 to 60	1	0	0.0%
61 to 70	2	2	100.0%

Early in the same year Banks [4] in England also reported twenty-five cases treated with the Ferry antitoxin with seven deaths, a case fatality rate of 28 per cent.

Inspired by these favorable reports, we decided to use the new meningococcus antitoxin. The plan was to give meningococcus antitoxin or antimeningococcus serum to alternate patients admitted without regard to the severity of the disease or to the age or sex of the patient. The method of treatment and dosages were the same as those already outlined for antiserum. Seventy-six patients were treated in this way, forty-three with antiserum and thirty-three with antitoxin. The difference in the numbers of cases treated is explained by the fact that patients transferred from general hospitals, where antiserum had already been given, were continued on antiserum, usually of the same make as that previously used.

RESULTS

Eighteen of the forty-three patients treated with antimeningococcus serum died, a case fatality rate of 41.8 per cent. Of the thirty-three meningococcus antitoxin-treated patients fourteen died, a case fatality rate of 42.4 per cent. If patients who died within forty-eight hours of admission are considered insufficiently treated, the rate is 30.6 per cent for the antiserum and 24.0 per cent for the antitoxin.

It is apparent from a comparison of the percentage mortality rates in table 1 that meningococcus antitoxin was no more beneficial than an effective brand of antimeningococcus serum in the treatment of epidemic cerebrospinal meningitis. However, judging from the percentage of deaths occurring within forty-eight hours, it appears that the cases treated with antitoxin were, on the whole, more severe than those treated with the antiserum.

A study of table 2, arranged in ten year groups and respective fatality rates, shows that antiserum and antitoxin were given to equally unfavorable subjects. The youngest patient in these two groups of cases was 3 months and the oldest 64 years old, averaging 14.2 years. The average age of the patients treated with antitoxin was 15.6 years and the average of those treated with antiserum was 13.2 years.

COMPARISON OF OUR RESULTS WITH THOSE OF HOYNE

Our case fatality rate of 41.8 per cent in cases treated with antiserum compares favorably with the 45.9 per cent cited by Hoyne,[2] but our rate of 42.4 per cent is nearly twice as high as the 23.5 per cent reported by him in his antitoxin-treated cases. The explanation for this difference in results is not obvious. An analysis of factors involved in the therapy of this series of cases fails to reveal any specific reason.

The meningococcus antitoxin used by us was obtained from the same firm [5] that supplied Hoyne with material for the treatment of his eighty-five cases.

Our method of intrathecal therapy differed from that of Hoyne. We gave alternate lumbar and cisternal injections of the antitoxin every twelve hours during the first thirty-six or forty-eight hours, then followed with one injection daily, by the lumbar route. Hoyne gave lumbar injections once daily, using the cisternal method only when there was a block in the lower route. The fact that our fatality rate among cases treated with antimeningococcus serum compares favorably with that reported by Hoyne seems to indicate that our method of intrathecal treatment was not a factor acting against a favorable rate in the antitoxin-treated cases.

The amount of antitoxin given by us seems to have been adequate. A study of table 3 shows that the average amount of antitoxin administered intrathecally and intravenously in our series of successfully treated cases exceeded that given by Hoyne.

That the answer to this question depends wholly on the therapeutic value of the antitoxin itself may be derived from experience in the use of antimeningococcus serum. It is generally known that standard brands of antimeningococcus serum may vary widely in their therapeutic value and that even an effective brand may fail to produce uniformly good results in a given epidemic.

TABLE 3.—*Amount of Meningococcus Antitoxin Received by Patients Who Recovered in Our and in Hoyne's Series of Cases*

	Total Average	Smallest Amount	Largest Amount	Average Amount Parenteral Administered	Average Amount Intrathecal Administered
Our series	283.0 cc.	145.0 cc.	620.0 cc.	132.0 cc.	151.0 cc.
Hoyne's series	161.7 cc.	75.0 cc.	360.0 cc.	58.5 cc.	115.1 cc.

This is likely to be true in epidemics occurring in different parts of the country. It is believed to be due to the difference in the strains of meningococci prevailing in a particular epidemic and the strains used in developing the antibacterial serum. Gordon [1] discarded standard brands of antimeningococcus serum and succeeded in lowering the mortality rate in the 1927 to 1931 epidemic in Detroit by the use, among other measures, of an antiserum developed through immunizing horses with the prevailing strains of the meningo-

2. Hoyne, A. L.: Meningococcic Meningitis: A New Form of Therapy, J. A. M. A. **104**: 980 (March 23) 1935.

3. Ferry, N. S.; Norton, J. F., and Steele, A. H.: Studies of the Properties of Bouillon Filtrate of the Meningococcus: Production of a Soluble Toxin, J. Immunol. **21**: 293 (Oct.) 1931.

4. Banks, H. S.: Note on Ferry's Meningococcus Antitoxin in the Treatment of Acute Cerebrospinal Fever, Lancet **1**: 856 (April 13) 1935.

5. Meningococcus Antitoxin, Parke, Davis & Co., Detroit, New and Nonofficial Remedies, J. A. M. A. **104**: 1007 (March 23) 1935.

coccus. Wright and his colleagues [6] stated that, when a patient with meningococcic meningitis fails to respond to treatment, one cannot justifiably conclude that the strain of organism encountered is resistant to serum therapy but only that the serum used is not specific for that organism.

Branham [7] expressed the opinion that various lots of antitoxin undoubtedly vary in efficacy, as do those of antibacterial serum, and this will result in conflicting reports of its value until such time as standardization becomes more satisfactory.

Therefore it seems logical to conclude that our less successful results were due in part or wholly to the difference in action of the meningococcus antitoxin itself.

SULFANILAMIDE

In the spring of 1937, among the many startling reports on the curative power of sulfanilamide, was one by Schwentker and his associates [8] on ten cases of meningococcic meningitis and one of meningococcemia. Recovery occurred in all but one of the cases of meningitis, indicating the effectiveness of the drug against human infection as well as experimental infection in mice reported earlier by Buttle [9] and confirmed by Rosenthal and his associates.[10]

Encouraged by these reports, we decided to include meningococcic meningitis on our list [11] of diseases for treatment with sulfanilamide. The routine method of treatment already described was in no way to be changed except that sulfanilamide would be substituted for antiserum and antitoxin and that intrathecal injections (lumbar) would be given once a day until two negative spinal fluid cultures were obtained.

DOSAGES

The doses of sulfanilamide are summarized in table 4.

The initial dose of sulfanilamide is calculated on the basis of 15 grains (1 Gm.) per 20 pounds (9 Kg.) of body weight up to 100 pounds (45 Kg.). Above this weight it is rarely necessary to exceed a total of 90 grains (6 Gm.). We believe it is important to obtain, as soon as possible, blood and spinal fluid concentration of from 10 to 15 mg. or more of the drug per hundred cubic centimeters and to keep the concentration at this level with adequate maintenance doses. It is better, it seems to us, to err on the side of too large rather than too small doses. We have had patients whose blood and spinal fluid reached a level of 25 mg. of the drug without causing any deleterious effects. Depending on the method of administration, the maintenance dose should be given either every four or eight hours, day and night, during the acute stage of the disease. This procedure is followed until the patient has shown unmistakable signs of improvement. The night doses are then omitted. The daily doses must be continued well into convalescence, usually for from seven to ten days, if relapses are to be avoided.

A check on the level of the drug in the blood should be made from four to eight hours after the large initial dose to determine whether satisfactory concentration has been reached. If found below the desired level, the next maintenance dose should be doubled, followed in four hours by the regular maintenance dose by mouth. Another determination of the blood level of the drug is advised at the end of twenty-four hours. This is to check on the adequacy of the maintenance doses.

Sulfanilamide is excreted principally through the kidneys. Consequently, to maintain a high and even concentration the fluid intake should be restricted to about 2,000 cc. in twenty-four hours in adults, and proportionate amounts in children.

Sulfanilamide is given in tablets or crushed in water or milk. An equivalent amount of sodium bicarbonate should be given with each dose of sulfanilamide in order to avoid acidosis. This condition is apt to develop in infants and young children. We have seen it in two of our small children. For parenteral administration, a solution containing 1 per cent of sulfanilamide in physiologic solution of sodium chloride or one-sixth molar sodium lactate is used. When the latter is utilized, sodium bicarbonate is unnecessary.

If the initial dose of the drug is administered by venoclysis, the first maintenance dose by mouth should be given immediately afterward rather than after four hours. This is advisable because of the rapid excretion of the drug by the kidneys as a result of diuresis, which usually follows venoclysis.

TABLE 4.—*Doses of Sulfanilamide in the Treatment of Epidemic Cerebrospinal Meningitis*

Tablets for Administration by Mouth

During Acute Stage of the Disease

	Initial Dose	Maintenance Dose	Intervals (Day and Night)
Adults (100 lbs. and over)	50-90 gr.	15-20 gr.	4 hrs.
Adults (50-90 lbs.)	30-50 gr.	10-15 gr.	4 hrs.
Children (25-50 lbs.)	20-30 gr.	5-10 gr.	4 hrs.
Babies	10-20 gr.	5 gr.	4 hrs.

During Convalescence	Maintenance Dose	Intervals
	10-15 gr.	Four times daily
	5-10 gr.	Four times daily
	5 gr.	Four times daily

One per Cent Solution of Powdered Sulfanilamide in Physiologic Solution of Sodium Chloride or in One-Sixth Molar Sodium Lactate for Parenteral Administration During Acute Stage of the Disease

	Initial Dose	Maintenance Dose	Intervals
Adults (100 lbs. and over)	700 cc.	500 cc.	8 hrs.
Adults (50-90 lbs.)	300-500 cc.	200-300 cc.	8 hrs.
Children (25-50 lbs.)	100-300 cc.	100-200 cc.	8 hrs.
Babies	100 cc.	100 cc.	8 hrs.

Intrathecal Administration

5 to 10 cc. less than amount of cerebrospinal fluid removed

METHODS OF SULFANILAMIDE THERAPY

The treatment of epidemic cerebrospinal meningitis has been based principally on the premise that the antimeningococcus serum, in order to be effective, must come in direct contact with the organisms in the meninges. This necessitated the introduction of the serum directly into the subarachnoid space by way of the lumbar region, cisterna magna or the lateral ventricles.

Since the World War the administration of antibacterial serum intravenously in addition to the intrathecal injection has been generally used on the theory that meningococcemia precedes the meningitis. It has been the belief, however, that little or no antiserum reaches the meninges when given intravenously or subcutaneously.

In 1935 Hoyne [2] predicted that eventually it would be shown to be entirely unnecessary to administer any

6. Wright, I. S.; DeSanctis, A. G., and Shepler, Adele: The Determination of the Value of Serum in the Treatment for Meningococcus Meningitis, Am. J. Dis. Child. **38:** 730 (Oct.) 1929.
7. Branham, Sara E.: Serum, Antitoxin and Drugs (Sulfanilamide) in Treatment of Meningococcus Meningitis, M. Ann. District of Columbia **7:** 1-5 (Jan.) 1938.
8. Schwentker, F. F.; Gelman, Sidney, and Long, P. H.: The Treatment of Meningococcic Meningitis with Sulfanalamide: Preliminary Report, J. A. M. A. **108:** 1407-1408 (April 24) 1937.
9. Buttle, G. A. H.; Gray, W. H., and Stephenson, Dora: Protection of Mice Against Streptococcal and Other Infections by P-Aminobenzenesulfonamide and Related Substances, Lancet **1:** 1286-1290 (June 6) 1936.
10. Rosenthal, S. M.; Bauer, Hugo, and Branham, Sara E.: Studies in Chemotherapy: Comparative Studies of Sulfonamide Compounds in Experimental Pneumococcus, Streptococcus and Meningococcus Infections, Pub. Health Rep. **52:** 662 (May 21) 1937.
11. Stevens, R. E.: Sulfanilamide in the Treatment of Other Bacterial Infections, Rhode Island M. J. **21:** 145-148 (Oct.) 1938.

serum intrathecally if sufficient antitoxin was injected intravenously. A year later he [12] reported ninety-six cases treated exclusively by intravenous injections of antitoxin with a fatality rate of 15.9 per cent.

The advent of sulfanilamide has placed this method of treatment of epidemic cerebrospinal meningitis on a more rational basis. Banks [13] and Willien [14] had reported the cure of meningococcic meningitis with sulfanilamide given by mouth or subcutaneously without intrathecal administration. Marshall and his associates [15] reported that they had found sulfanilamide in all body fluids, including the spinal fluid, when the drug was given by hypodermoclysis as well as by mouth. Allott [16] found that the concentration of the drug in the spinal fluid was very nearly that in the blood. We arrived at the same conclusion after a large number of tests.

These facts, together with the relatively simple technic [17] for determining the concentration of the drug in the spinal fluid and blood, make the intravenous, subcutaneous or oral therapy of meningococcic meningitis entirely feasible. Lumbar puncture is done only for the purpose of diagnosis and drainage. Consequently we changed our original method of sulfanilamide therapy. At first we reduced gradually the number of intrathecal injections and finally omitted all but one injection following the first diagnostic lumbar puncture.

istration or by Levine tube, if necessary, every four hours (day and night) during the acute stage of the disease. In mild cases the administration of sulfanilamide in adequate doses by mouth is sufficient.

RESULTS OF SULFANILAMIDE THERAPY

Since the spring of 1937, twenty-nine cases of epidemic cerebrospinal meningitis have been treated entirely with sulfanilamide. This plan of treatment with sulfanilamide has been continued in spite of the fact that experimental [18] and clinical reports [19] have indicated that the combined use of the drug and antibacterial serum or antitoxin is more effective against meningococcic infection than sulfanilamide alone. Our justification for the continuance of this plan is the fact that our results have been very satisfactory. Also there are clinical reports [20] showing good results in the use of sulfanilamide alone in the treatment of meningococcic meningitis.

Five of the twenty-nine patients died, a fatality rate of 17.2 per cent. Four of these were in the group of nineteen patients who received daily intrathecal injections as well as parenteral and oral administrations of the drug, and all these deaths occurred within twelve hours of admission to the hospital. The other death was in the group of eight patients who received but one intrathecal treatment in addition to the parenteral and oral therapy and took place fifty-one hours after admission. Two patients who were treated entirely by oral administration of the drug recovered.

TABLE 5.—*Influence of Age on Results of Antiserum, Antitoxin and Sulfanilamide Therapy*

	Cases			Deaths			Fatality Rates			
	Antiserum	Antitoxin	Sulfanilamide	Antiserum	Antitoxin	Sulfanilamide	Antiserum	Antitoxin	Sulfanilamide	All Cases
Under 1 year	4	2	3	0	2	0	0.0%	100.0%	0.0%	22.2%
1 to 5 years	13	10	5	5	2	1	38.4%	20.0%	20.0%	28.6%
6 to 10 years	6	5	4	4	0	2	66.6%	0.0%	50.0%	40.0%
11 to 20 years	12	6	6	7	4	1	58.3%	66.6%	16.6%	50.0%
21 to 30 years	7	4	7	3	3	0	42.9%	75.0%	0.0%	33.3%
31 to 40 years	5	4	2	2	1	1	40.0%	25.0%	50.0%	36.4%
41 to 50 years	2	1	1	1	1	0	50.0%	100.0%	0.0%	50.0%
51 to 60 years	1	0	1	0	0	0	0.0%		0.0%	0.0%
61 to 70 years	1	1	0	1	1	0	100.0%	100.0%		100.0%
Totals	51	33	29	23	14	5	45.1%	42.4%	17.2%	37.1%

Because of the seriousness of epidemic cerebrospinal meningitis, we consider it imperative that measures to combat this disease be instituted with as little delay as possible. It follows that any method which could quickly bring the concentration of the drug to the optimum level in the blood and spinal fluid should be used. To do this we inject a 1 per cent solution of the drug into the spinal canal at the initial lumbar puncture and immediately follow this with a large dose intravenously or by hypodermoclysis. This helps to raise the blood and spinal fluid level rapidly. It also helps guarantee an adequate concentration against the possibility of poor absorption in the gastrointestinal tract, vomiting or other mishaps which may occur in the management of severely sick and uncooperative patients. When this is accomplished the optimum concentration of the drug is maintained by oral admin-

Excluding the four deaths within twelve hours, the corrected case fatality rate was 4.0 per cent. This result was impressive. It should be explained that these twenty-nine patients were admitted toward the end of the epidemic when the severity of the disease was decreasing, whereas those treated with antiserum and antitoxin were seen at the peak of the epidemic in 1935 and 1936.

Except for two small children who developed acidosis, there was no serious reaction to sulfanilamide. In no case was the drug discontinued because of its toxic action.

12. Hoyne, A. L.: Intravenous Treatment of Meningococcic Meningitis with Meningococcus Antitoxin, J. A. M. A. **107:** 478 (Aug. 15) 1936.

13. Banks, H. S.: Serum and Sulfanilamide in Acute Meningococcal Meningitis: A Preliminary Survey Based on One Hundred and Thirteen Cases, Lancet **2:** 7-13 (July 2) 1938.

14. Willien, L. J.: Sulfanilamide Therapy in Meningococcic Meningitis, J. A. M. A. **110:** 630-632 (Feb. 26) 1938.

15. Marshall, E. K. J.; Emerson, Kendall, Jr., and Cutting, W. C.: Para-Aminobenzenesulfonamide: Absorption and Excretion; Method of Determination in Urine and Blood, J. A. M. A. **108:** 953-957 (March 20) 1937.

16. Allott, E. N.: Sulfanilamide Content of Cerebrospinal Fluid During Treatment, Lancet **2:** 13-14 (July 2) 1938.

17. Schmidt, E. G.: The Determination of Sulfanilamide in Tungstic Acid Blood Filtrates by Means of Sodium Beta-Naphthoquinone-4-Sulfonate, J. Biol. Chem. **122:** 757-762 (Feb.) 1938.

18. Branham, Sara E., and Rosenthal, S. M.: Studies in Chemotherapy: Sulfanilamide, Serum, and Combined Drug and Serum Therapy in Experimental Meningococcus and Pneumococcus Infections in Mice, Pub. Health Rep. **52:** 685-695 (May 28) 1937. Brown, T. M.: Protective Action of Sulfanilamide and Antimeningococcus Serum on Meningococcus Infection in Mice, Bull. Johns Hopkins Hosp. **61:** 272 (Oct.) 1937. Branham, Sara E.: The Effect of Sulfapyridine and Sulfanilamide With and Without Serum in Experimental Meningococcus Infection, Pub. Health Rep. **55:** 12-24 (Jan. 5) 1940.

19. Waghelstein, J. M.: Sulfanilamide in the Treatment of One Hundred and Six Patients with Meningococcic Infections, J. A. M. A. **111:** 2172 (Dec. 10) 1938. Clyde, W. A., and Neely, M. G.: Clinical Experience in the Treatment of Meningococcemia and Meningococcic Meningitis: Analysis of One Hundred and Eighteen Cases Treated with Four Different Methods of Treatment, South. M. J. **32:** 594-601 (June) 1939. Banks.[13]

20. Bryant, Joseph, and Fairman, H. D.: Chemotherapy of Cerebrospinal Fever in the Field, Lancet **1:** 923-926 (April 22) 1939. Buttle, Gray and Stephenson.[9] Willien.[14]

ANALYSIS OF ENTIRE SERIES

There were forty-two deaths in the entire series of 113 cases, a case fatality rate of 37.1 per cent. Exclusion of the twenty-two deaths occurring within forty-eight hours of admission brings the fatality rate down to 21.9 per cent.

The influence of age on the fatality rate in epidemic cerebrospinal meningitis has been generally considered to be most favorable in the group between 6 and 10 years old and very unfavorable under 1 and over 50 years. Analysis of results in table 5 shows the youngest age group to be the most favorable with two deaths in nine cases, a rate of 22.2 per cent. The next favorable group is the 1 to 5 year group, with eight deaths in twenty-eight cases, a rate of 28.5 per cent. The expected favorable age group of 6 to 10 years has a fatality rate of 40.0 per cent.

It is admitted that statistics based on a small number of cases are subject to error and therefore inconclusive. They are presented here primarily for the sake of completeness.

In all but four of the 113 cases, diagnosis of epidemic cerebrospinal meningitis was confirmed by recovery of the organism either from the spinal fluid or from the blood. The four cases in which meningococcus was not found were diagnosed from the clinical observations alone. These were so definite and typical that a diagnosis of meningococcic meningitis was considered justifiable.

COMPLICATIONS AND RELAPSES

There were two complications in the entire series of 113 cases. One was paralysis of the external rectus muscle of one eye, which developed during the acute stage of the disease. The patient was a woman who was treated with meningococcus antitoxin. The other was total deafness in a child 2 years of age who was treated with antimeningococcus serum.

One relapse was encountered in a youth aged 20 years who had been treated with antiserum. He had recovered from the meningitis in five days. Twelve days later he developed meningococcemia. He recovered after a long period of treatment with antiserum, antitoxin, autogenous vaccine and finally sulfanilamide.

SUMMARY

One hundred and thirteen cases of epidemic cerebrospinal meningitis, representing for the greater part a small epidemic, were treated with antimeningococcus serum, meningococcus antitoxin and sulfanilamide. The case fatality rate for the entire series was 37.1 per cent.

A special study comprising seventy-six cases was undertaken to determine the relative therapeutic values of antimeningococcus serum and the meningococcus antitoxin of Ferry. Forty-three cases were treated with antimeningococcus serum and thirty-three with meningococcus antitoxin with a fatality rate of 41.8 per cent and 42.4 per cent respectively. The result in the latter group was not as favorable as that reported by Hoyne. The reason for this is not obvious but appears to be attributable to the inadequate action of the antitoxin itself.

In a group of twenty-nine cases treated with sulfanilamide alone the fatality rate was 17.2 per cent. In the treatment of these cases intrathecal administrations of the drug were reduced to one in each of eight cases and none in two.

Complications were confined to one each of the antiserum and antitoxin-treated cases and none in the sulfanilamide. There was only one relapse and this was in an antiserum-treated case.

These data and our personal experience in the care of patients with epidemic cerebrospinal meningitis during the last five years have led us to draw the following conclusions:

1. The therapy of epidemic cerebrospinal meningitis with antimeningococcus serum and meningococcus antitoxin is, at best, inadequate. The number of deaths is high, irrespective of the amount of serum used and the methods of treatment employed.

2. The meningococcus antitoxin of Ferry has not been impressive clinically. The results obtained with this form of treatment have not been better than those with standard brands of antimeningococcus serum.

3. Sulfanilamide has been shown to be highly efficacious even when used alone. The clinical results are impressive and in some instances dramatic.

4. Sulfanilamide offers the best means by which the treatment of epidemic cerebrospinal meningitis can be simplified. The drug enters the subarachnoid space readily when given intravenously, subcutaneously or orally. This makes intrathecal administrations of the drug more of an expedient than a necessity.

THE DESIVAC PROCESS FOR DRYING FROM THE FROZEN STATE

EARL W. FLOSDORF, PH.D.
F. J. STOKES, M.A.
AND
STUART MUDD, M.D.
PHILADELPHIA

During the past few years, evidence has been accumulating which supports the value of human blood plasma or serum as substitutes for whole blood transfusion.[1] In the case of traumatic shock without hemorrhage where there is hemoconcentration, plasma may even be preferable to whole blood.[2] Even when there is no hemoconcentration, the advantage of a blood substitute not requiring matching of type and one readily available immediately in the emergency is clear. The reduction in hemoglobin which patients can endure without danger is extreme; it is reduction in circulating blood volume which must be corrected promptly. In cases of nephrosis and of increased cerebrospinal fluid pressure as resulting from concussion, the advantage of concentrated plasma or serum is added to the other advantages by virtue of an increased osmotic effect to withdraw fluids into the circulatory system. In dry form resulting from desiccation from the frozen state the plasma proteins may be maintained in highly stabilized form, without refrigeration except for long time reserve-storage, and are instantly available for use by dissolving in water to the original or to a more concentrated volume. Although these proteins may be stored either as plasma or as serum, it appears that the former may be preferable by virtue of minimizing the danger of reactions.[3]

War-time emergency increases the importance of ready availability of large reserves of this agent in the

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The length of this article does not permit an extensive review of the literature, but from the key references cited a full bibliography may be obtained.

1. Strumia, Max M.; Wagner, Joseph A., and Monaghan, J. Frederick: The Use of Citrated Plasma in the Treatment of Secondary Shock, J. A. M. A. **114**: 1337 (April 6) 1940.
2. Moon, Virgil H.: Circulatory Failure of Capillary Origin, J. A. M. A. **114**: 1312 (April 6) 1940.
3. Strumia, Max M.; Wagner, Joseph A., and Monaghan, J. Frederick: The Intravenous Use of Serum and Plasma, Fresh and Preserved, Ann. Surg. **3**: 623 (April) 1940.

dry stabilized form. However, the dosage for shock is large, 400 cc. being minimal. The aggregate volume of large numbers of such dosages brings out limitations of previously employed processes of desiccation from the frozen state, e. g. the lyophile [4] and the cryochem [5] procedures. Accordingly, we will describe a new process which has particular advantage in processing on the large scale required, the desivac process, which has been on trial in our laboratories for several years.

In the lyophile process the water vapor is removed in vacuum by condensers maintained at the temperature of solid carbon dioxide, —78 C. A pressure well under 0.2 mm. is maintained. In the cryochem process a regenerable chemical desiccant, specially prepared calcium sulfate, is used for removal of water vapor. The pressure can be as high as from 1 to 2 mm.

The difference in critical degree of vacuum of the lyophile and cryochem processes reveals that this factor is a function of the efficiency of the means for removing water vapor. The desiccant in the latter process is more efficient than low temperature condensation, permitting a higher operating pressure. Accordingly, with still more efficient means for removal of water vapor, a yet higher critical pressure might be expected to be possible, permitting direct vacuum pump connection with evaporating frozen material.[6] To provide properly efficient means of water removal requires that the water be removed from the pump continuously with maintenance of the oil at a low vapor pressure.

We have accomplished this by use of pumps of large volumetric capacity which circulate the oil used in the vacuum seal rather than by ordinary pumps which operate in a static bath of oil. The oil from the exhaust or atmospheric side of the pump is passed continuously through a device for separation of water from oil, a continuously operating centrifuge. The water is separated in liquid phase from the oil-water emulsion and the clarified oil is returned directly to the high vacuum side of the pump. In this way, oil of low vapor pressure is continuously available for the high vacuum seal of the pump, and the water vapor is withdrawn from the high vacuum space, as rapidly as it is evaporated, directly to the atmosphere and is discharged there in the liquid phase. This system is so efficient that it will operate at 4.5 mm. of mercury pressure and still keep the materials frozen solid by loss of the latent heat of evaporation. By the end of the drying cycle the pump finally produces a pressure below 200 microns, which readily removes the last traces of water from the material being desiccated so that the residual moisture content is brought well below 1 per cent.

Degassing and self freezing may be employed [5] or the materials may be prefrozen before evaporation is started. In the former case only about half as much material may be desiccated with a given size apparatus because a much greater amount of water must be evaporated in order to freeze the material as compared with that necessary merely to maintain the frozen state during desiccation. However, by employing an external cooling means, even if insufficient in itself for freezing, the procedure of degassing and self freezing may be made much more efficient than otherwise and the step of freezing is accomplished most quickly and with less manipulation than by external prefreezing.

The material to be desiccated may be treated in bulk or in the final containers as previously described.[7] In the latter case the containers may be placed on an external manifold and sealed as previously described.[8] The metal desitube or can containers appear to have definite advantage for the purposes already described.[9]

The containers may be arranged within a vacuum chamber more conveniently, however, for large scale operation. Because of vacuum insulation, degassing and self freezing operates much more efficiently. When combined with external cooling, operation becomes exceedingly simple.

In order to complete desiccation rapidly, it is desirable to circulate warm water in a jacket in the vacuum chamber to supply the heat of vaporization more rapidly, by increasing the temperature of the radiating source within the metal chamber. Such heating was not necessary in the original methods of Shackell [10] or Craigie [11] with glass desiccators and is not necessary when the final containers are on an external manifold.[7] In the latter case the contents are adjacent to the walls of the containers which are in direct contact with the atmosphere, so that heat input is sufficiently rapid.

For breaking the vacuum at the completion of the process, an arrangement is provided for passing the air to the chamber through the dry-air sterilizer previously described,[5] except that it is one of larger size and is attached directly to a single large valve. The containers are removed and sealed when on external manifolds of the cryochem apparatus or are placed in desitubes.

The chambers may be designed for sterilization by use of steam at 15 pounds pressure. Also sight-glasses are easily provided for watching the progress of drying, reading thermometers, and the like. Equipment is available for desiccation of from 10 to 100 liters daily in a single apparatus. For these large capacities it is lower in initial cost and operation than either the cryochem or the lyophile apparatus.

Although this process is superior for large scale operation in production of blood substitutes, the cryochem process is preferable for smaller scale operation, as in smaller hospitals, particularly up to 1 liter capacity. The quantities of desiccant required are small and its regeneration is exceedingly simple. We have recently improved the cryochem apparatus so that the desiccant and containers of material to be dried are all within a single chamber. The arrangement of these containers with relation to finally admitting dry sterile air and so on is exactly as described in connection with the desivac process. On regeneration of the desiccant the entire apparatus is sterilized, and the dry-air sterilizer built in the apparatus is reconditioned. During drying, the heat of reaction of the water vapor with the desiccant is utilized as the source of heat for evaporation; this may be supplemented by electrical sources, thermostatically controlled by the temperature of the desiccant.

When it becomes necessary to adsorb ethanol and other organic ingredients from solutions being dried, silica gel may be used. This frequently is an advantage. It also permits external prefreezing by immersing the containers in low temperature baths without concern for the solvent adhering to the outer walls of the con-

4. Flosdorf, Earl W., and Mudd, Stuart: Procedure and Apparatus for Preservation in "Lyophile" Form of Serum and Other Biological Substances, J. Immunol. **29:** 389 (Nov.) 1935.

5. Flosdorf, Earl W., and Mudd, Stuart: An Improved Procedure and Apparatus for Preservation of Sera, Micro-Organisms and Other Substances—The Cryochem Process, J. Immunol. **34:** 469 (June) 1938.

6. Except at a higher pressure, the low mass per unit volume of vapor would require use of impracticably large pumps.

7. Flosdorf and Mudd, footnotes 4 and 5.

8. Flosdorf, E. W.; Boerner, F.; Lukens, M., and Ambler, T. S.: Cryochem-Preserved Complement of Guinea Pig Serum, Am. J. Clin. Path. **10:** 339 (May) 1940. Flosdorf and Mudd, footnotes 4 and 5.

9. Flosdorf, Boerner, Lukens and Ambler.[8]

10. Shackell, L. F.: An Improved Method of Desiccation, with Some Applications to Biological Problems, Am. J. Physiol. **24:** 325 (June) 1909.

11. Craigie, James: A Method of Drying Complement from the Frozen State, Brit. J. Exper. Path. **12:** 75 (April) 1931.

tainers. Although in the cryochem process silica gel is only one half as efficient for water vapor as calcium sulfate per equal weight of desiccant, or one fourth per equal volume [12] (based on aqueous tension of desiccants as determined by maintenance of frozen state during desiccation), the two desiccants may be mixed in order to obtain the superior capacity of calcium sulfate for water. Ten pounds of silica gel will adsorb 20 Gm. of ethanol satisfactorily.

SUMMARY

The desivac process, a new process for vacuum desiccation from the frozen state, is more economical than earlier procedures for vacuum drying on the large scale required, for instance in the preservation of human blood plasma for use as a blood substitute. It is entirely mechanical in operation; the water vapor is removed directly from the high vacuum space and is discharged to the atmosphere in the liquid phase. Low temperature condensation or chemical desiccants are not required.

Improvements in the cryochem process for use in smaller laboratories have been made.

Clinical Notes, Suggestions and New Instruments

HYPERTENSION IN A 7 YEAR OLD GIRL WITH WILMS' TUMOR RELIEVED BY NEPHRECTOMY

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The work of Goldblatt,[1] Page [2] and others has shown that hypertension may be produced experimentally in dogs and monkeys by effecting a relative ischemia of one or both kidneys. There are many ways in which clinical pathology might simulate the experimental methods of these workers. Blatt and Page [3] have studied a case of lymphosarcoma with hypertension apparently due to constriction of both renal arteries by the tumor mass.

Ratliff,[4] Crabtree [5] and McIntyre [6] have reported hypertension in patients with unilateral, chronically infected kidney lesions. Of this group Goldblatt has said,[7] "It becomes probable that the hypertension associated with unilateral or bilateral pyelonephritis in children and adults occurs only in those cases in which there is associated vascular sclerosis or in which the inflammatory disease produces the same effect on renal circulation as does vascular disease." The reported cases of this type which have come to surgery have been uniformly relieved of hypertension.

Recent reviews of the subject of Wilms' tumor, notably those of Priestley and Broders,[8] and of Bothe,[9] have made no mention of blood pressure reading.

We wish to present the case of a little girl in whom marked hypertension seems to have been due to unilateral interference with circulation of the kidney by a tumor of the kidney itself.

12. Volume of desiccant is important with respect to size of the vacuum chamber.

1. Goldblatt, Harry: Experimental Hypertension Induced by Renal Ischemia, Harvey Lecture, Bull. New York Acad. Med. **14:** 523-553 (Sept.) 1938.

2. Page, I. H.: The Production of Persistent Arterial Hypertension by Cellophane Perinephritis, J. A. M. A. **113:** 2046-2048 (Dec. 2) 1939.

3. Blatt, Ebner, and Page, I. H.: Hypertension and Constriction of Renal Arterioles in Man: Case (Due to Lymphosarcoma), Ann. Int. Med. **12:** 1690-1699 (April) 1939.

4. Ratliff, R. K.: Hypertension of Unilateral Renal Origin, Univ. Hosp. Bull. Ann Arbor **5:** 42-43 (June) 1939.

5. Crabtree, E. G.: High Blood Pressure in Destructive Infected Unilateral Lesions of the Kidney, Tr. Am. A. Genito-Urin. Surgeons **31:** 299-319, 1938.

6. McIntyre, D. W.: Unilateral Chronic Pyelonephritis with Arterial Hypertension: Apparent Cure After Nephrectomy, J. Urol. **41:** 900-905 (June) 1939.

7. Quoted by McIntyre.

8. Priestley, J. T., and Broders, A. C.: Wilms' Tumor: A Clinical and Pathological Study, J. Urol. **33:** 544-551 (June) 1938.

9. Bothe, A. C.: Tissue Changes in Mixed Tumors of Kidney After Irradiation, J. Urol. **33:** 434 (May) 1935.

REPORT OF CASE

C. W., a white girl aged 7 years, entered the Methodist Hospital Feb. 26, 1940, on the service of Dr. Karl M. Koons, with a history of swelling in the upper part of the abdomen, nontender, noted by her mother seven weeks previously. For the past three or four weeks the child had rested after coming home from school instead of playing as had been her previous habit. No other symptoms were elicited.

The past and the family history were irrelevant except for tonsillectomy in June 1939, at which time her blood pressure was recorded as 120 systolic, 70 diastolic.

The child was rather pale, active and alert. She was 49 inches (124.5 cm.) tall and weighed 47 pounds (21.3 Kg.); on examination the temperature was 100 F., the pulse rate 96 and the respiratory rate 20.

The physical abnormalities were confined to the abdomen. There was a visible tumor in the left upper quadrant which on palpation was firm, only slightly irregular, partially movable, extending up under the rib margin, across the midline and 3 or 4 cm. below the umbilicus. There was no tenderness. The first blood pressure reading, recorded February 28, was 180 systolic, 130 diastolic.

Laboratory examinations revealed the following: Specific gravity of the urine was 1.009, with a very faint trace of albumin; it was alkaline and showed no pus or blood. The blood showed: hemoglobin content 12.5 Gm., or 82 per cent, red blood cells numbered 4,070,000, white blood cells 4,650, polymorphonuclears 60 per cent, eosinophils 1 per cent, small lymphocytes 39 per cent. Coagulation and bleeding time six minutes.

February 27 an x-ray examination of the kidney, ureter and bladder and an intravenous pyelogram revealed a tumor of the upper pole of the left kidney, apparently malignant.

Dr. J. H. P. Gauss saw the patient as a consultant, and immediate operation was decided on, the preoperative diagnosis being Wilms' tumor of the left kidney. A discussion of operation versus roentgen therapy is of great interest but is outside the scope of this paper.

The blood pressure February 29 at 9 a. m. was 156 systolic, 126 diastolic and at 9 p. m. 190 systolic, 155 diastolic.

March 1, under avertin with amylene hydrate-ethyl chloride-ether anesthesia, a left paramedian incision was made; the peritoneum was incised laterally, the kidney freed, and the vessels and the ureter clamped, ligated and cut. Enlarged glands extended out from the pelvis of the kidney and along the aorta and vena cava. One nodule was noted in the under surface of the left lobe of the liver, and no effort was made to remove any of the glands. A transfusion of citrated blood had been started during the operation, and the patient was never in shock. Ten minutes after the operation the blood pressure was 135 systolic, 65 diastolic.

The postoperative course was uneventful. The pulse, which before operation had averaged 96, averaged 120 during the remainder of the hospital stay. The temperature came down to normal on the third day and remained constantly so after the sixth day. Blood pressure readings were as follows: March 2, 130 systolic, 80 diastolic; 3d, 125 systolic, 75 diastolic; 4th, 104 systolic, 68 diastolic; 5th, 125 systolic, 85 diastolic; 6th, 120 systolic, 60 diastolic; 8th, 130 systolic, 90 diastolic; 9th, 128 systolic, 68 diastolic; 10th, 120 systolic, 80 diastolic; 11th, 116 systolic, 76 diastolic. The patient was discharged in good condition on the eleventh postoperative day.

ABSTRACT OF PATHOLOGIC REPORT

The specimen consisted of a tumor mass and kidney 15.5 by 10 by 9 cm. There was a small, firmly circumscribed portion apparently of kidney tissue, although on section the architectural markings were not apparent. On section the tumor itself was very soft and yellowish gray, with small areas of hemorrhagic infiltration. There were a few cystlike cavities filled with a yellowish, gelatinous fluid. Microscopically there was seen fairly normal kidney tissue; then as the tumor was approached this blended into a very firm fibrous tissue, finally blending into the tumor itself, which was made up of compactly arranged round cells, irregular as to size, shape and staining qualities. There was no definite architecture; the stroma consisted of fine fibrous connective tissue.

Farther away from the kidney substance there were areas of marked inflammatory reaction with numerous polymorphonuclears and necrotic cellular débris. The pathologic diagnosis was embryoma of the kidney (Wilms' tumor).

COMMMENT

The exact mode of interference with renal circulation is not apparent but was probably due to pressure of the tumor tissue invading the renal pedicle and adjacent lymph nodes. The compactness of the tissues in that area was most evident at operation, before the kidney was freed from its bed. Another possibility was that the neoplastic mass which almost entirely surrounded the kidney acted in the same manner as the cellophane envelope used by Page[2] to produce experimental hypertension.

The hypertension could scarcely have been due to some product of the tumor itself as metastases were found, yet the blood pressure returned to normal level.

CONCLUSION

In the case here presented of a child with marked hypertension apparently due to unilateral interference with renal circulation by Wilms' tumor, the hypertension was relieved by nephrectomy.

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A SIMPLE, EFFECTIVE, FABRIC RESTRAINT-SPLINT

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A simple muscular ankle and wrist restraint has been effectively used as a restraint-splint in the care of patients with acute anterior poliomyelitis and may be used to advantage in many other conditions. In addition to its simplicity it is inexpensive, can be made universally available and can be used repeatedly.

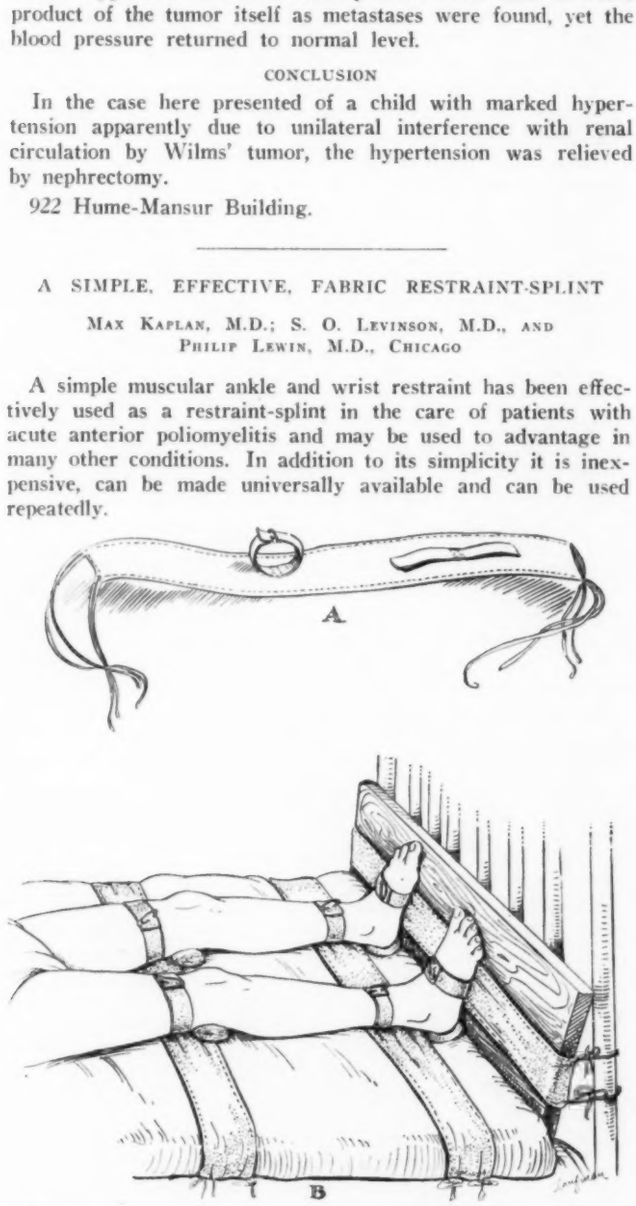

Fig. 1.—Combination restraint and bandage splint. *A*, showing bandage splint made of heavy cloth with two short strips of cloth attached. One strip made into loop and secured with safety pin. Note ties at ends of cloth. *B*, three restraint and bandage splints in positions. Note rolls under knees and cotton "doughnuts" under heels. Pads for the soles of the feet are not shown. The combination of this bandage and Carrell's Bradford frame and hinged restraint is excellent.

The indication for its use is as a temporary substitute for the generally used plaster and metal splints for the extremities. In mild cases of poliomyelitis in which there is no paralysis or only slight paresis of muscles of the extremities, the restraint-splint may be used throughout the acute and subacute stages of the disease.

The purpose of the restraint-splint is to immobilize and comfortably restrain the extremities in order to achieve support, protection against fatigue and overstretching of weakened muscles, and neutralization of antagonist muscle-pull, thus preventing deformities and contractures.

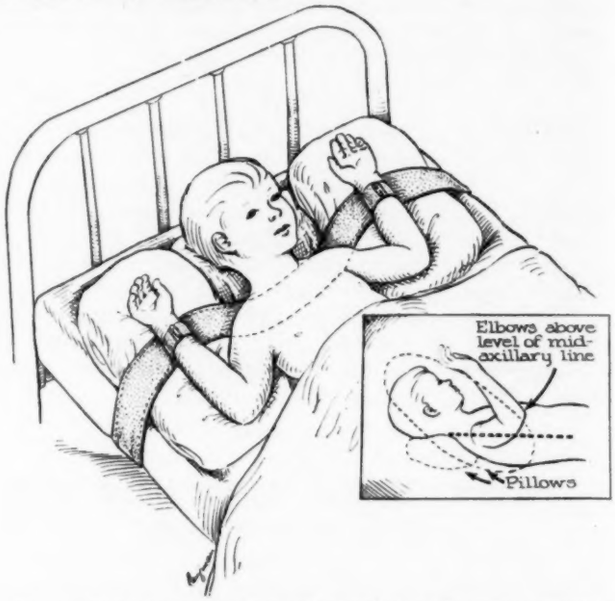

Fig. 2.—Restraint and bandage splint applied to the upper extremities maintaining the physiologic position of neutral muscle pull. Note the pillows, the bandage and the wristlets. The inset indicates the relationship of the arm to the patient's body.

The article consists of a double thickness band of unbleached muslin 6 inches in width and approximately 36 inches in length, hemmed along its four edges. Two shorter strips of muslin about 2 inches in width are sewed, approximately 18 inches apart, on the muslin band in its long axis. Each of these "loop-strips" is attached at its middle, thus leaving the ends free to be looped around an extremity, like a wristlet or anklet, and fastened with a safety-pin. Attached to the corners of the large muslin band are streamers of ordinary cloth bias tape approximately 30 inches in length, which are tied to the sides of the bed or around the foot-support (placed to maintain the feet in dorsiflexion), thus stretching the restraint-splint tautly and securing it in place.

The technic of application to the lower extremities is as follows: The patient is placed on his back with a small flat pillow under the lumbar spine and a small "roll" under each knee. A cotton "doughnut" is placed under each heel. Three restraint-splints are placed across the bed, beneath the patient, at the following levels: (1) around the foot support, (2) just above the ankle, (3) just above the knee. Occasionally, one placed at the midthigh level will be found useful and effective. The tape-streamers are then tied securely to the bed under the spring and mattress or about the foot-support, stretching the restraint-splint flat and taut. The "loop-strips" are placed around the extremities at the various levels and fastened snugly, but not tightly, with safety-pins. Those for the feet are placed around the arch and fastened over the dorsum, thus preventing rotation of the foot and leg, and eliminating sand bags and other bulky devices (fig. 1).

The application to the upper extremity is shown in figure 2, in which is also illustrated the ease and convenience with which the restraint-splint is used in conjunction with pillows as supports.

The advantages of the restraint-splint are ease of manufacture, universal availability, low cost, ease of laundering and sterilizing, ease and simplicity of application. Since so little of the skin surface is covered by the loops, a great part of the patient's skin can be bathed and powdered without the restraints being removed. Furthermore, extremities encased in plaster casts or padded aluminum splints during warm weather become hot, sweaty and uncomfortable. These objections are eliminated to

a great extent by this type of splint. The simplicity of removal and application results in a minimum of disturbance and discomfort to the patient during skin care and toilet. In addition, there is no loss or breakage.

COMMENT

The restraint-splint works very well in conjunction with other devices such as the Bradford frame, the Carrell-Girard frame, the Toronto-LeMesurier splints and split mattresses.

The dimensions of the restraint-splint may be varied according to the size of the patient and the anatomic level at which the restraint is to be placed. The distance between the "loop-strips" may be shortened and thus be made to fit any patient by making a fold at the middle of the large band and securing the fold with safety-pins.

The restraint-splints should be laundered well, ironed without starch and autoclaved after being used. They may be stored or carried ready for use by folding and enclosing them in paper, cloth or cellophane wrappers, each one appropriately labeled according to its purpose; viz., "child," "adult," "upper extremity," "lower extremity." Thus they can be made readily available in every hospital, doctor's and health officer's bag.

The entire restraint-splint can be improvised from an old sheet or towel and a ball of twine or some shoe laces and ten safety-pins. It can be used in a respirator, a farm house or an automobile trailer. It can be made economically in large quantities by Red Cross or WPA workers or by any volunteer organization.

This restraint was designed by Misses Blake, Robeson and Black, the supervisors and instructors of pediatric nursing in Michael Reese Hospital, after a careful survey of restraints used elsewhere. It has been used successfully for restraining a child during the administration of parenteral fluids and other medical and surgical procedures. However, the combination and arrangement of several restraints, as herein described, to form what we call the restraint-splint, have not been to our knowledge used or described before.

They may be effectively used in a variety of conditions and situations where temporary or moderate immobilization is necessary; viz., burns, osteomyelitis, fractures, postoperatively and during the transition period following the removal of braces, casts and splints.

The simplicity of the restraint-splint and the relative ease of large quantity manufacture may well render it useful at the battle front during the periods of transportation and temporary care of the wounded. Injured extremities can be rapidly immobilized with this type of restraint-splint, which can be used on a stretcher as well as on a hospital bed.

We should like to call it the Michael Reese restraint-splint, with the notation that it was first used for poliomyelitis patients by Dr. Kaplan.

A PRACTICAL SUBSTITUTE FOR GLASS COVERSLIPS

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My attention has been recently directed to the problem of finding some suitable material that could be used to replace the glass coverslip. Formerly the slips have been imported from Germany, England and Japan. The war has seriously threatened the supply of them, and the price has increased from $1.50 to $3.75 an ounce. These factors make the imported slips almost prohibitive to the average hospital laboratory.

After trying various substances, my attention was fortunately directed to plastacele which is made by the E. I. DuPont Company, 626 Schuyler Avenue, Arlington, N. J. Plastacele is perfectly transparent. Regular size coverslips can be easily cut from it with ordinary scissors or any other type of suitable cutting instrument.

Sheets of plastacele can be ordered in various sizes. Ordinarily a sheet measuring 20 by 50 inches will allow about 1,000 coverslips and cost about $1 a sheet. Order No. C-12-7511.

Coverslips of plastacele are satisfactory for microscopic urinalysis, fecal smears and such purposes. Tissue slides can also be mounted with it, and undoubtedly other uses will be found for them as time passes on.

810 Doctors Building.

Council on Industrial Health

MEDICAL SERVICE IN INDUSTRY

THE COUNCIL ON INDUSTRIAL HEALTH HAS APPROVED THIS ARTICLE AS ONE OF A SERIES ON MEDICAL SERVICE IN INDUSTRY WHICH WILL APPEAR FROM TIME TO TIME IN THE JOURNAL.

C. M. PETERSON, Secretary.

INTRODUCTION

Large industrial establishments in this country are classified as those which employ more than 500 workers. Many business organizations of this size have found medical supervision over employees, materials, processes and working conditions to be a practical necessity. This trend gains strength as industrialists learn by education and example that maintenance of trained manpower at gainful employment uninterrupted as far as possible by disability from injury or illness is good business. It is possible to demonstrate, as many physicians have done over long periods of time and in all kinds of manufacturing operations, that industrial medical departments can be conducted without compromise of ethical or scientific medical standards and yet in excellent conformity with the purposes of industry. Once this view is widely accepted by industry and the medical profession, greater demand for the services of physicians as a means for conserving the health of workers may be expected.

Distribution of Industrial Establishments According to Number of Employees

Establishments Employing	Number of Establishments	Number of Wage Earners
Number of wage earners	6,885	.....
1 to 5 wage earners	62,164	170,174
6 to 20 wage earners	46,402	514,487
21 to 50 wage earners	23,138	750,922
51 to 100 wage earners	11,911	852,373
101 to 250 wage earners	9,745	1,522,670
251 to 500 wage earners	3,911	1,363,000
501 to 1,000 wage earners	1,660	1,333,323
1,001 to 2,500 wage earners	737	1,080,534
2,501 or more wage earners	241	1,181,748
Totals	166,794	8,569,231

U. S. Census of Manufacturers, 1937.

These demands will probably come soonest from large firms able individually to support adequate medical facilities, yet which have for various reasons failed to develop them. A more important demand should come from small manufacturing units and other commercial enterprises, once a means is found for providing an adequate service which they can with advantage support. The accompanying table describes the distribution of industrial establishments classified according to the number of wage earners employed.

Frequently there is great need for medical service in these small plants, the more so since it is unrealized and since unfavorable sickness or accident experience is not in any sense a function of plant size. The Council on Industrial Health believes that these needs represent a considerable opportunity for medical achievement and that this demand should be encouraged and controlled through the establishment of an educational service which will:

1. Acquaint physicians with the special character of industrial medicine, surgery and hygiene and the necessity for the enforcement of standards defining scope and professional competence.

2. Convince employer and employee alike that medical service in industry merits support only as it is soundly organized economically, scientifically and ethically and that to produce lasting benefits it must be satisfactory both to those who provide and to those who receive the service.

Manufacturers' associations, trade unions, insurance carriers and compensation and other governmental agencies have large and legitimate interests in the workers' safety and health. All are actively engaged in establishing economic, social and humanitarian values of control over industrial accident and disease. In view of this widespread interest the ability of medical organizations to exert a constructive influence on industrial health standards takes on added significance, since other agencies are

not in good position to evaluate medical procedure or facilitate direct application of improved knowledge or technic into actual practice. To relinquish leadership in any program involving the public health to extraprofessional agencies is out of keeping with medical tradition long established in other specialty fields. Principal reliance for improved industrial health standards must rest on medical education and self discipline administered through the physicians' own organizations. The Council on Industrial Health of the American Medical Association was established as a means of focusing attention from all elements in the medical profession on industrial health problems. For identical reasons cooperating committees on industrial health are being organized in the medical societies of states where the nature or concentration of industry appear to justify such a step.

FUNCTIONS OF STATE COMMITTEES ON INDUSTRIAL HEALTH

A program has been developed as a guide to committees on industrial health in state medical associations which has the following well defined objectives:

1. To train industry and labor to the value of industrial health conservation.
2. To develop a clear understanding of the proper scope and functions of industrial medicine and to clarify relationships between private and industrial practice.
3. To keep the medical profession informed about all accepted methods for reducing the frequency and severity of industrially induced disability.
4. To elevate medical relations under workmen's compensation.
5. To scrutinize all legislation affecting the health of industrial workers.
6. To improve relationships between medicine and insurance.
7. To establish working relationships with all agencies in the state interested in industrial health.
8. To arrange for the adoption of similar activities through cooperating committees in the medical societies of the industrial counties.

To accomplish these objectives it has been recommended that the personnel of the state committees include representation from:

1. Private practice.
2. Industrial medical practice.
3. Medical representation if such exists from each of the following:
   (*a*) State bureau of industrial hygiene.
   (*b*) State workmen's compensation agency.
   (*c*) The medical faculties in the state.
   (*d*) Industrial insurance company.

A bulletin has been developed by the Council on Industrial Health to permit interchange of ideas between committees of the state societies and as a means of estimating progress.

COUNTY MEDICAL SOCIETY ORGANIZATION

The adoption of similar objectives and methods of organization by cooperating committees in county medical societies provides a sound basis for mobilizing community resources for general or special industrial health activity in accordance with local needs. Under such a plan it should be possible to establish competent sources of information about the character of local industrial operations and the important health problems of each as a first step toward early recognition and control. The resources of other community organizations interested in industrial health need investigation in order to determine how they may contribute to physical betterment of workers under enlightened medical leadership. There will be many opportunities to promote better professional training. The general public can be informed of accomplishments in industrial practice and their effect on the health of the community as a whole. An excellent means is provided whereby the interdependence of private and industrial practice is demonstrated and the activities of both augmented by consulting services in industrial hygiene developed by governmental and private agencies. Working relationships can be promptly established with the allied professional groups—industrial hygienists, safety engineers and industrial nurses.

Recent developments indicate that county society committee organization of this character can contribute materially to the provision of industrial health services for the small plant owner and his employees interested in deriving benefit from advances in industrial medicine, surgery and hygiene but who in the past have found themselves unable to do so. Most important, it establishes a direct means of assistance to the physician who wants to know how he should conduct himself for greater and more competent participation in this field.

Council on Physical Therapy

THE COUNCIL ON PHYSICAL THERAPY HAS AUTHORIZED PUBLICATION OF THE FOLLOWING REPORTS. HOWARD A. CARTER, Secretary.

CONTINENTAL ULTRA SHORT WAVE UNIT MODEL SW-100, ACCEPTABLE

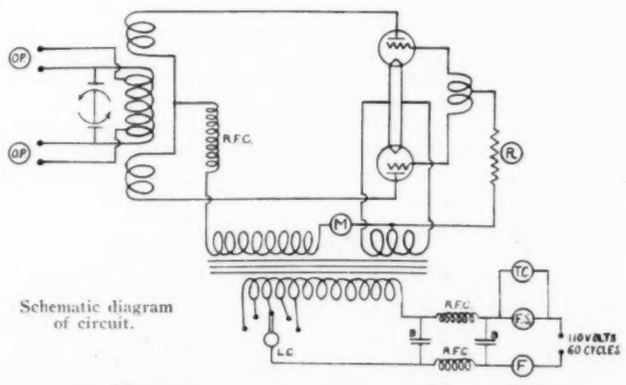
Distributor: Bedford Surgical Company, Inc., 1326 Fulton Street, Brooklyn.

The Continental Ultra Short Wave Unit, Model SW-100, is used for medical and surgical diathermy. Pads, cuffs, inductance coil, surgical accessories and metal electrodes are supplied as standard equipment. The shipping weight of the unit is 120 pounds.

Continental Ultra-Short Wave Unit, Model SW-100.

The firm states that the unit operates on approximately 6 meters and utilizes two tubes in a self-rectifying, push-pull, tuned plate, tuned grid oscillating circuit. The patient's circuit is inductively and capacitatively coupled to the oscillating circuit and is controlled by a split stator condenser in parallel. In tests performed by the Council the power input was found to be 750 watts and the output 280 watts; transformer temperature was 76.3 C. after the unit had been operated at full load for two hours. This temperature comes within the limits of safety prescribed by the Council.

Three radio frequency chokes incorporated in the circuit are said to reduce radio interference.



Schematic diagram of circuit.

The firm submitted data to substantiate claims for heating tissues, which were confirmed by the Council's investigation. The data are as follows:

CUFFS

Technic: Size of cuffs, 2 by 14½. Space under cuffs: Test 1, 1 inch; other tests, 1¼ inches. Space between cuffs: Test 1, 7½ inches; other tests, 7 inches. Average thigh circumference 20 inches. Average room temperature 83 F. Average room humidity 65 per cent.

Average Temperature (F.) of Six Tests

	Cutaneous	Subcutaneous	Intramuscular	Rectal
Initial	91.96	94.68	97.88	99.6
Final	99.1	103.25	106.23	99.9

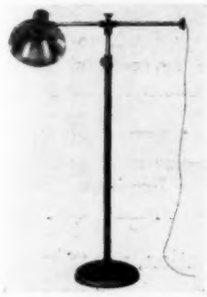
The Council's clinical investigation of the unit revealed that it gave satisfactory clinical service.

The Council voted to accept the Continental Ultra Short Wave Unit, Model SW-100, for inclusion in its list of accepted devices.

GENERAL AUTOMATIC E-40 LAMP ACCEPTABLE

Manufacturer: General Automatic Corporation, Macedonia, Ohio.

The General Automatic E-40 Lamp is an infra-red generator. The source of radiation is mounted in a reflector having a polished metal reflecting surface. The reflector is 10½ inches in diameter and is placed on an adjustable stand. The maximum height of the stand is 71½ inches and the minimum collapsed height is 48 inches; the horizontal adjustment is 24 inches. Power input of the lamp is 260 watts. The weight is 24 pounds.



General Automatic E-40 Lamp.

The firm submitted data concerning the distribution of energy of the lamp compiled by a reliable investigator.

The lamp was investigated clinically by the Council and it was found to give a very intense heat at what is considered a comfortable distance with other infra-red lamps. If placed at a greater distance or angled away from the area to be treated the heat is then comfortable and pleasant. It is necessary to exercise caution when using this lamp owing to the intense heat. It is easy to focus the heat on the patient with the adjustable arm and can be used for either side of the patient without carrying the lamp from one side to the other, as the extension is long enough for this purpose. The lamp is bottom heavy and will not tip easily.

Advertising submitted by the firm consisted of a folder which contained a description of the lamp. No therapeutic claims are made and the folder appears acceptable.

The Council voted to accept the General Automatic E-40 Lamp for inclusion on its list of accepted devices.

OTARION HEARING AID ACCEPTABLE

Manufacturer: Otarion Inc., 448 North Wells Street, Chicago.

The Otarion Hearing Aid was given consideration by the Council and its investigation revealed that:

The instrument consists of the following parts:

(*a*) Combined microphone and vacuum tube amplifier unit. Single control switch.

(*b*) A and B batteries enclosed in leatherette carrying case.

(*c*) Crystal midget receiver with molded earpiece.

The microphone and amplifier unit is in a flat molded case 3½ by 2⅜ by ¾ inches, weighing 88 Gm. The control is a sliding contact on the edge of the instrument.

Otarion Hearing Aid.

The A battery is a single No. 1, ES 1½ volt Burgess dry cell. The measured current drain is 41 milliamperes. The B battery is a 45 volt Burgess R 30 battery. The current drain is 0.54 milliampere. The A battery is carried in a metal sheath in the flap of the Otarion.

Mechanical Features.—The instrument is simple in construction, neat and workmanlike in appearance. The tests for amplification show that while the instrument is not uniform over the whole frequency range, in view of the limitations of a miniature amplifier, it provides a fair approximation to uniformity. The tests showed that the instrument gave appreciable amplification at 8,192 cycles.

Carrying Case.—Replacement of both A and B batteries is easily effected. The overall dimensions of the battery case are 4½ by 3 by 1⅛ inches; total weight, 350 Gm.

Internal Noise.—The instrument is quiet for all settings of the volume control less than about three fourths full on. Above this the instrument is subject to feed back squeal unless the molded earpiece is fitted very well.

Amplification.—The following overall amplifications were shown:

	128	256	512	1,024	2,048	4,096
At normal ear threshold ⅔ full on	nil	16	23	40	43	26
At normal ear threshold ¼ on....	nil	nil	20	33	30	22
At approximately 45 decibels above normal threshold, ⅔ full on....	nil	12	12	25	23	21

The Council on Physical Therapy voted to accept the Otarion Hearing Aid for inclusion on its list of accepted devices.

ROSE "QUARTZ-X" ULTRAVIOLET LAMP ACCEPTABLE

Manufacturer: E. J. Rose Manufacturing Company, Inc., 727-733 East Gage Avenue, Los Angeles.

The Rose "Quartz-X" Ultraviolet Lamp produces ultraviolet radiation and is in the general class of "cold" or low pressure ultraviolet generators.

A transformer, time clock, cable attachment and line cord are located in the base of the lamp. At the top of an adjustable telescoping column rising from the base is a horizontal arm which pivots about the vertical axis of the center column. It also carries a pivot to which is attached a second arm supporting the burner. A dome shaped hood made of molded plastic covers the burner terminals. The two burners supported by the aluminum reflector are parallel and consist of tubing 8 mm. in diameter. One tube is made of fused quartz and the other ultraviolet transmitting glass designated as "Corning 972 UlV." (Corex).

Rose "Quartz-X" Ultraviolet Lamp.

In the center of the hood, at the back, is a three position switch lighting either the quartz, corex or both burners. The diameter of the hood is 33 cm. and the reflector is recessed 5 cm. below the rim.

The following evidence concerning the physical characteristics of the lamp was submitted by the firm:

Power consumption (on 110 volts) in watts, and the intensity of therapeutic ultraviolet radiation in microwatts per square centimeter at 24 inches were as follows:

Quartz burner	75 watts	345 microwatts
Corex burner	76 watts	156 microwatts
Both burners	94 watts	435 microwatts

During a three hour test no part of the lamp or transformer case became heated.

The spectral distribution was measured by the ultraviolet photometer and found to be:

Quartz	Corex	Both				
88.5	62	88	Between	2,000	and	2,600
10	34	10.5	Between	2,600	and	3,000
1.5	4	1.5	Between	3,000	and	3,200

in percentage of the total energy in wavelengths less than 3,200 angstroms. Physiologic tests on untanned abdominal skin gave minimum perceptible erythema in the following time:

Quartz burner	90 seconds
Corex burner	240 seconds
Both burners	75 seconds

The Council investigation confirmed these results and showed that the lamp is acceptable as a mercury glow "cold" type lamp. The spectrograms and the transmission data on the glass used in the corex tube show that the ultraviolet output is changed but little from that of the quartz tube.

On submission for the Council's consideration the lamp was named the Rose "Whole Spectrum" Ultraviolet Lamp. When advised by the Council that the name "Whole Spectrum" would not be acceptable, the firm changed the name of the unit to "Quartz-X." The Council was notified of this change by the firm April 25, 1940.

The Council voted to accept the Rose "Quartz-X" Lamp for inclusion on its list of accepted devices.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, SEPTEMBER 28, 1940

THE PLATFORM OF THE AMERICAN MEDICAL ASSOCIATION

The American Medical Association advocates:

1. The establishment of an agency of the federal government under which shall be coordinated and administered all medical and health functions of the federal government exclusive of those of the Army and Navy.

2. The allotment of such funds as the Congress may make available to any state in actual need, for the prevention of disease, the promotion of health and the care of the sick on proof of such need.

3. The principle that the care of the public health and the provision of medical service to the sick is primarily a local responsibility.

4. The development of a mechanism for meeting the needs of expansion of preventive medical services with local determination of needs and local control of administration.

5. The extension of medical care for the indigent and the medically indigent with local determination of needs and local control of administration.

6. In the extension of medical services to all the people, the utmost utilization of qualified medical and hospital facilities already established.

7. The continued development of the private practice of medicine, subject to such changes as may be necessary to maintain the quality of medical services and to increase their availability.

8. Expansion of public health and medical services consistent with the American system of democracy.

THE COORDINATING COMMITTEE FOR MEDICAL PREPAREDNESS

An executive order was issued on September 19 setting up, with the approval of the President, under the Council of National Defense, a subordinate body to the council to be known as the Medical and Health Committee. The chairman of this organization is Dr. Irvin Abell, who is also chairman of the American Medical Association's Committee on Medical Preparedness. The order defining the establishment of the committee and its duties follows:

Pursuant to the authority vested in it by section 2 of the act of Aug. 29, 1916 (39 Stat. 649), the Council of National Defense, with the approval of the President, hereby establishes as a subordinate body to the council a committee to be known as the Health and Medical Committee. The committee shall consist of the following members: Dr. Irvin Abell, who shall be chairman, the Surgeon General of the Army, the Surgeon General of the Navy, the Surgeon General of the Public Health Service, and the chairman of the Division of Medical Sciences of the National Research Council. Vacancies occurring in the membership of the committee shall be filled by appointment by the council with the approval of the President. The members of the committee and of such subcommittees as may be formed by the committee shall serve as such without compensation but shall be entitled to actual and necessary transportation, subsistence and other expenses incidental to the performance of their duties.

It will be the responsibility of the committee to advise the Council of National Defense regarding the health and medical aspect of national defense and to coordinate health and medical activities affecting national defense. In carrying out its functions the committee may (*a*) utilize, to the extent that such facilities are available for such purpose, the laboratories, equipment and services of the Medical Departments of the Army and Navy, of the Public Health Service and of other government institutions and (*b*) within the limits of the appropriations allocated to it, to contract with and transfer funds to such institutions and to enter into contracts and agreements with individuals or educational or scientific institutions for studies, experimental investigations and reports.

The committee shall promulgate rules and regulations for the conduct of its work, which rules and regulations shall be subject to the approval of the council and the President.

This executive order brings to a favorable conclusion a cause for which officials of the Association, representing the Board of Trustees and the House of Delegates, have labored persistently since the annual session in June. The work of the American Medical Association in the development of personnel for the military services, for industrial medicine and for maintaining the health of the people can be carried forward with far greater efficiency through the establishment of some relationship directly with the government. The work of the National Research Council in the investigation of procedures to be carried out for military purposes, in the development of information to be circulated to the medical profession and in the standardization of military medical procedures will also be greatly facilitated by this coordinating committee.

No doubt announcements will issue in the near future from the coordinating committee indicating the nature of its activities and the cooperation that will be required from the medical profession. Under the leadership and with the membership of the committee that has been established, the medical profession may give to this committee its complete confidence and an assurance of full cooperation.

MEDICAL CARE AND REFUGEE CHILDREN

Already many children of British scholars have come to this country and are under the care of American teachers in institutions of higher education who have volunteered their assistance. In some instances physicians have wished to participate in this charitable activity, and a few have written to THE JOURNAL requesting information as to how they may secure the children of British physicians. For the present, all such activities are being conducted by the United States Committee for the Care of European Children, Inc., 215 Fourth Avenue, New York City. This agency will give any physician who is especially interested, and who will write to it, specific information.

A physician in an Ohio community was called to attend a small child who had been brought to this country from England for placement in an American home to escape the dangers of war. This physician found that the child was suffering from badly diseased tonsils and adenoids. He recommended an operation but was advised that the surgical procedures contemplated could not be undertaken lawfully until consent was obtained from the child's parents in England. As more and more European children are placed in American homes the problem that confronted this physician will necessarily constantly recur. Any unnecessary delay in providing medical care for the children would be most unfortunate. The United States Committee for the Care of European Children, in which now centers the responsibility of securing American homes for the young refugees, has given this matter of authorization of medical care considerable thought. The committee realizes the importance of the matter and is working on a plan to effect a definite solution to the problem. Pending the completion of this plan, however, the committee thus expresses the view that there need not now be any such delay as was suggested to the Ohio physician:

> Pending a more permanent arrangement, the United States Committee and any foster parents, however, are not left completely remediless. We feel that there is a degree of factual background which would enable a foster parent, on the basis of general American law, to consider himself as acting in loco parentis. Among such factors are that the English parents of their own volition sent their child to an American home and assumed all the risks inherent therein, that the American foster parents have taken the child into their home, have supported it, have cared for it, and generally have exercised custodial powers over it. Certainly, it would seem such foster parents could exercise their rights over the child as against any other individuals, with the exception of the child's actual parents. Bearing such factors in mind it would appear likely that American courts would hold that the American foster parent, having assumed all these rights, duties and obligations, would likewise have the power to consent to any necessary medical or surgical treatment of the child.
>
> We feel that there are also two further mitigating circumstances. In the first place it is highly unlikely that the question would ever be raised except by the English parents themselves and it is extremely doubtful, in view of all the circumstances, that they would complain. In the second place, we feel that an American court would be reluctant to hold the United States committee or the foster parents liable for such a given consent when the whole picture of this emergency child care movement was adequately and forcefully presented. If, on the other hand, the foster parents were negligent in handling the matter they should be held liable.

If an American family which receives a European child into its home agrees in so doing to furnish the child with the necessities of life, as probably is the case, there may arise a question of legal responsibility if a delay in furnishing medical care, certainly one of the necessities of life, results in injury to the child even though that delay may be occasioned by uncertainty as to the right on the part of the foster parents to authorize the needed medical or surgical attention. This whole matter, while only one of the many problems incident to the evacuation of European children to this country, is of sufficient importance to justify the hope that whatever doubts may now exist as to the right to give a valid authorization for the rendering of necessary medical care to the children may be removed without delay.

BODY BUILD AND HYPERTENSION

While the prevailing opinion assumes a constitutional factor in hypertensive diseases, there is no unanimity of opinion on the relation between gross body structure and blood pressure. Robinson and Brucer [1] based their study of this question on a statistical analysis of the periodic health examination records of 3,658 unselected men and women (age concentration of the 1,861 males between 31 and 55 years, that of 1,797 females between 27 and 50 years) who were classified into linear, or narrow chested, and lateral, or broad chested, groups by means of a simple anthropometric index found by dividing chest circumference by standing height and ignoring body weight. Persons of linear build were defined as having a chest/height ratio of less than 0.50, their chest measurement being less than half their height; those of lateral build showed on the average an index of 0.59 or over. A gradual increase in chest circumference was noted for both men and women before the age of 50, with a decrease thereafter. Extremely large chests were not observed in the old age groups. This suggests a high death rate in men with large chests during the previous decades. Men of linear build with chest/height ratios of 0.47 and under showed an average systolic pressure of 114 mm. and an average diastolic pressure of 70 mm. In the average lateral type man the systolic pressure was as high as 130 mm., the diastolic 79 mm. The median and modal systolic pressures rose from 110 mm. in men of linear build to more than 118 mm. in those of lateral constitution; median and modal diastolic pressures rose from 70 mm. in the linear body type to over 77 mm. in the lateral. The tendency in women was similar.

The difference in susceptibility to hypertension in persons of contrasting body build extremes was unusual. Only 4 per cent of the men of linear body structure had systolic pressures over 140 mm., whereas 22 per cent of the laterally built men were definitely hypertensive. Only 2 per cent of the women of the linear type as compared with 27 per cent of those of the lateral type had systolic pressures over 140 mm. Forty-three per cent of the men of linear build but only 17 per cent of those of lateral build had low diastolic pressures under 70 mm., while 60 per cent of the women of the linear constitution but only 34 per cent of those of lateral build showed a similar diastolic trend. Low blood pressures of either kind were accordingly found predominantly in persons of linear body structure and high pressures in the opposite type. Men of the lateral, or broad chested, type had more than four times the expectancy of systolic hypertension and

1. Robinson, S. C., and Brucer, Marshall: Body Build and Hypertension, Arch. Int. Med. **66**: 393 (Aug.) 1940.

seven times that of diastolic hypertension than men of linear, or narrow chested, gage.

In women the ratio was even more striking, an eleven times greater systolic hypertension expectancy and an eight times greater diastolic hypertension expectancy in those of the lateral type. Moreover, persons of broad build showed higher pressures than persons of narrow build at all age levels. Men of linear build did not show an increased systolic pressure until late in life, women not until after the age of 50. Men of linear type maintained about the same diastolic pressure throughout life. Women of the linear type showed an increase in mean diastolic pressure but not to so great an extent or at such a high level as women of the lateral type. Accordingly the incidence of low systolic pressure was high among persons of the linear build at every age as compared with that of persons of the opposite body build. Diastolic pressures showed much the same tendency. Since the authors believe in a correlation of hypertension with the lateral, or broad, build and of low pressure with the linear, or thin, build they regard the hereditary predisposition to normal pressure and hypertension as an established fact.

Current Comment

PLAGUE IN THE UNITED STATES

The first recorded appearance of plague in the United States occurred in San Francisco on March 6, 1900. In reviewing developments in this country since that time, Hampton [1] points out that human cases of the disease have been reported in eight states in the following chronologic order: California 1900, Washington 1907, Louisiana 1914, Florida 1920, Texas 1920, Oregon 1934, Utah 1936 and Nevada 1937 (the last human case was reported from Millard County, Utah, on Dec. 4, 1939). In all, 499 human cases with 314 deaths were recorded between 1900 and Jan. 1, 1940. Between 1934 and 1939, however, only fifteen cases of plague with six deaths have been reported in the United States, and all of these but four cases and one death occurred in California. This record exists in spite of the fact that plague infection has been demonstrated in fourteen species of ground squirrels and in red squirrels, tree squirrels, flying squirrels, wood rats, kangaroo rats, field mice, prairie dogs, chipmunks, marmots and one cotton tail rabbit, in addition to the more common infection in rats. The reason this widespread sylvatic distribution has not resulted in more human cases may be in part explained by the sparse human settlements in those regions of extensive wild life infection. However, as records already available show, wild rodent plagues may spread unnoticed over wide areas unless intensive measures are taken to detect their presence. Further spread of the infection eastward through a rodent and human population of insufficient density to give rise to explosive epidemics may, however, eventually bring the disease within striking distance of the rat and human populations of large cities. Here the disease may become epidemic in the presence of a sufficiently high population of rats and a sufficiently high flea index to provide favorable conditions for human infection. Furthermore, as rightly emphasized, the relatively small number of cases of plague during the past forty years does not indicate that too much prominence has been accorded that disease, since its ability to surmount the barrier of quarantine, its persistence and gradual biologic and geographic spread and the difficulty of eradicating it must continue to place it high in the rank of public health problems. The extensive available knowledge of plague prevention and control and the exercise of constant vigilance should guarantee, however, that it need not be permitted to occur in epidemic form in any locality in the United States.

1. Hampton, Brock C.: Plague in the United States, Pub. Health Rep. **55**: 1143 (June 28) 1940.

INFANTILE BERIBERI IN HONG KONG

According to a report by Fehily,[1] an investigation at the Infant Welfare Center in Hong Kong revealed that 18 per cent of the infants on first admission showed clinical signs of beriberi, placing this disease immediately after respiratory and cutaneous disorders in order of frequency. It was further found on examination that 81 per cent of those breast fed by mothers whose milk was peroxidase negative (a specific test for vitamin B_1 avitaminosis) were found to show signs of infantile beriberi of varying severity. Previous experiments, Fehily points out, have shown that the milk of women with a B_1 avitaminosis is not only deficient in this vitamin but also actively toxic. Others have succeeded in isolating methylglyoxal from the milk and urine of B_1 avitaminotic women, which may, it is suggested, represent the toxic factor. Although presumably vitamin B_1 deficiency is more common in Hong Kong than in most sections of this country, the observations made there may prove of great value everywhere.

PHYSIOLOGY OF INTERCOSTAL NERVE

The physiologic explanation for the appearance of abdominal symptoms in the presence of thoracic disease, the most notable of which is the referred pain over the appendix sometimes actually resulting in unnecessary surgery, has not been entirely clear. Kahn,[1] in a recent report based on investigations of the intercostal nerves of dogs, found that stimulation of the central end of any intercostal nerve causes a reflex inhibition of respiration and effects a concomitant drop in blood pressure. The lower intercostal nerves (seventh to twelfth) elicit a greater response than do the upper ones. Likewise it was shown that stimulation of sensory or intercostal fibers in the diaphragm causes reflex contraction of the abdominal musculature through a reflex connection with other lower intercostal nerves. These observations contribute to the understanding of the physiologic mechanisms involved in referred pain and the muscular rigidity in the lower abdominal quadrant resulting from involvement of the base of the lung by various pathologic processes.

1. Fehily, Lydia: Infantile Beriberi in Hong Kong, the Caduceus (University of Hong Kong) **19**: 78 (May) 1940.

1. Kahn, A. J.: Studies on Intercostal Nerve Physiology, Proc. Soc. Exper. Biol. & Med. **44**: 514, 1940.

MEDICAL PREPAREDNESS

In this section of The Journal each week will appear official notices by the Committee on Medical Preparedness of the American Medical Association, announcements by the Surgeon Generals of the Army, Navy and Public Health Service, and other governmental agencies dealing with medical preparedness, and such other information and announcements as will be useful to the medical profession.

MEDICAL PARTICIPATION IN SELECTIVE SERVICE

CHARLES B. SPRUIT

Lieutenant Colonel (M. C.), General Staff Corps, United States Army; Medical Adviser to the Joint Army and Navy Selective Service Committee

Washington, D. C.

The nation through its representatives in Congress has again decided to increase the armed forces of the United States in accordance with a fair and just system of compulsory selection in order that the obligations and privileges of military training and service may be shared generally. The whole purpose of Selective Service is to procure men for our land and naval forces with a maximum of efficiency, economy and equity, and with a minimum of disturbance to the social, economic, industrial and agricultural life of the nation.

THE CHARACTER OF THE SELECTIVE PROCESS

The salient characteristic of selective service will be that of democracy in action. Men will be registered, classified and selected by boards composed of their neighbors who are empowered to determine for each registrant his liability for military service with fairness to him, the community and the nation. The state and national Selective Service headquarters will be directing and coordinating agencies.

THE OPERATION OF SELECTIVE SERVICE

In general terms, the operation of the Selective Service is as follows: On registration day all men between certain ages will register at their polling places. The registration cards will be numbered serially by local boards. A national lottery will be held in Washington to determine the order in which men in each local board area are liable for selection for military service. The board then sends questionnaires to the registrants. On a basis of his completed questionnaire, the board tentatively decides whether the registrant should be classified as available for military service or should be put in a deferred classification. If the board classifies him as available, it causes him to be examined by its examining physician; if found physically fit, he is definitely classified as available. The registrant may appeal his classification and have his appeal decided by a board of citizens of his state. National headquarters on advice from the armed services will issue a general call on each state to fill its quota. Each state headquarters will issue a similar call to each local board. The local board then selects the required number of available registrants in the order determined by the lottery and orders them to report at a fixed time to a military induction station. Each registrant who is physically and morally acceptable to the military is thereafter inducted into the military service.

EXEMPTIONS

The law provides in general that personnel of the armed services and alien diplomatic officials, consuls and consular agents shall not be required to register. Exemption from registration obviously precludes selection and induction.

It also provides for certain exemptions from service for ministers of religion and theological students in particular, and for persons who have completed or who are in process of completing certain years of service in the Regular Army or active National Guard. Persons in this category, however, must register.

DEFERMENTS

Provision has been made for the deferment, but not the exemption from service, of additional categories of persons generally stated as follows: (*a*) the Vice President, governors, legislators and judges of national and state governments; (*b*) any person holding an office whose continuance therein is found to be necessary in the maintenance of the public health, safety or interest; (*c*) those whose employment in industry, agriculture or other such occupation is found to be necessary to maintain national health, safety or interest; (*d*) those with dependents, and finally (*e*) those men found physically, mentally or morally deficient or defective.

DEFERMENTS FOR STUDENTS

A general deferment from induction for service and training has been provided during the school year 1940-1941 for any person who has entered on attendance in a course leading to a degree at a college or university which grants a degree in arts or science.

NO GROUP DEFERMENTS

The law specifically provides that no deferments will be made in the case of any individual except on the basis of the status of that individual, and further that no deferment shall be made of individuals by occupational groups or of groups of individuals in any plant or institution. It will thus be seen that the deferment of any individual whose exemption or deferment is not specifically provided by law will be decided by local boards on the merits of the case and the demonstration of the necessity for deferment. It is believed that such necessity can be demonstrated for residents and interns in hospitals, for key technical personnel in hospitals and laboratories and for officials in state, county and local health departments, and similar participants in matters of the public health.

CLASSIFICATION

Every registrant will be classified by local boards after due process into one of four general classes:

Class 1. Those available for service.

Class 2. Those deferred because necessary in a civil occupation.

Class 3. Those deferred because of dependent relatives.

Class 4. Those deferred by law or because obviously unfit for service.

THE ROLE OF THE PHYSICIAN

Inauguration of selective service brings a new responsibility to the medical profession and another opportunity of service to the nation. The role of the physician in the Selective Service mechanism will be

to examine, to find, to evaluate and to recommend. The local board and the appeal board will determine the final classification of all registrants. It is believed that the participation of the physician of the community in determining the physical qualifications of registrants will promote confidence in the fairness of the system and permit of a more accurate determination of the ability of a man to perform military service. The intimate knowledge that the local physician has of the members of his community should be of marked assistance not only in the determination of physical fitness but also in the detection of malingering on the part of men seeking to evade service.

There is a strong feeling in Congress and throughout the nation that, since men are being called to military service at great personal sacrifice, Selective Service officials should be men who are willing to make an important sacrifice by contributing voluntary service, and that a process based on devotion to the national interest should not deteriorate into a job holding organization. It appears very probable, therefore, that no compensation will be provided for members of local boards, boards of appeal, medical advisory boards, examining physicians or similar officials. Clerical employees will unquestionably be paid and will be thoroughly competent in order to free officials of petty clerical routine and leave them free to devote their time to their important responsibilities. Provision, however, has been made to furnish the supplies required in physical examination and to pay for those procedures necessary for the determination of a man's physical fitness, such as laboratory or x-ray examination.

PHYSICAL STANDARDS

It is the present intention of the armed services to accept for induction only those men who are fit for full duty. The physical standards of Selective Service, therefore, will be those of the using services, which in the case of the Army are substantially those now governing enlistments.

It is probable that all men inducted during the coming months will be sent to the Army for training and service. Army standards will accordingly be used. When men are required by the Navy and Marine Corps, the physical standards of those services will be issued and used. It is the general policy that men accepted by the Army for induction shall be immediately available for full training and service and be free from acute communicable disease.

Many physicians in the Selective Service process will be confronted with a new criterion of judgment. The doctor in civil life is concerned in treating his patients so that they may continue their present modes of living and physical endeavor. The criterion of judgment of Selective Service is that the man shall be capable of performing full military service in any type of organization. This criterion may be epitomized by stating that the man, after proper hardening, must be able to walk 15 or 20 miles, carrying 50 pounds on his back, without taking harm to himself in the process.

Since the decision as to the ability of any given registrant to perform such duty depends on the professional judgment of each physician who examines the man, it must be anticipated that there will be honest differences of professional opinion between the examining physicians of the local board and the examining physicians of the medical advisory boards; also between the examining physicians of Selective Service and the examining physicians on the military examining boards. These will be honest differences of opinion and must be expected and accepted. It is believed that they will be fewer than occurred in the World War, since the same standards of physical examination will be used by Selective Service and by the military examining boards.

LOCAL BOARDS

The basic responsibility of administration and determination will rest on the local boards, whose members will be selected from each of some 6,500 communities. These local boards will determine all deferments and exemptions and make the final and crucial classification, after local physical examination, which makes the registrant available for induction.

THE LOCAL EXAMINING PHYSICIAN

The physical examinations of Selective Service will be made by local examining physicians, who act as agents of the local boards for this purpose. When necessary, additional examining physicians may be appointed by the local board. The local examining physician will examine all registrants sent to him by the local board according to the standards of physical examination which will be furnished him. He will note all deviations from the normal on physical examination forms and then interpret them in the light of the physical standards and in terms of the ability of the registrant to perform full military service. Thereafter he will record his recommendations to the local board as to the physical qualifications of the man to do full or limited military service. If the registrant possesses defects that disqualify him for any military service, that fact likewise will be entered. In those cases in which the local board has appointed additional examining physicians, it may be feasible in certain communities to form an examining group to facilitate and expedite the examinations.

MEDICAL ADVISORY BOARDS

Medical advisory boards will be appointed by the President, on the recommendation of the state, to provide an agency of advice and assistance to examining physicians and to assist appeal boards in determining matters of physical fitness which have been appealed from the decision of the local board by the registrant or by the government agent. The medical advisory boards will as far as practicable comprise internists, ophthalmologists, otolaryngologists, orthopedists, surgeons, psychiatrists, clinical pathologists, radiographers and dentists.

MALINGERING

The experience of Selective Service during the last war showed the necessity of constant vigilance to detect malingering. Many men descended to self mutilation and numerous other more ingenious but less harmful subterfuges to escape military service. Malingerers will doubtless be encountered in the coming operation of Selective Service. Regulations on physical standards mention many of the more common practices used by malingerers to feign disability and describe methods by which these may be detected.

THE MEDICAL TASK

The fall increment of some 400,000 men will be distributed according to quotas to the several states and by each state headquarters to the local boards in that state. On the assumption that these 400,000 men will be equally divided among the 6,500 odd local examining boards, and utilizing the World War percentage of rejections by examining physicians of Selective Service

and of the Army, there will be about ninety men per local board for physical examination. As these men will not all be inducted immediately but will be called up during the following three or four months, the average examination load on each board will probably be between twenty and thirty men per month. These calculations are not applicable to each local board because the quota assigned to a local board takes into consideration certain credits to that community accruing from men presently in the regular services or active National Guard. The total appeals on physical grounds during the World War indicate a lesser load on medical advisory boards. The additional number of cases sent up for advice by local examining physicians is not known.

STATE HEADQUARTERS

The state headquarters operating under the governors of the several states are charged with the organization and operation of the Selective Service system within the respective states under the policies and procedures authorized by the President. For each state the President will designate one or more officers of the Medical Reserve Corps of the Army and Navy as medical assistants on the staffs of the several governors. They will assist the state authorities in the supervision and coordination of medical examinations throughout the state. They will establish and maintain liaison with all examining physicians and members of medical advisory boards, hold regional meetings for them to promote critical discussion and analysis of the medical problems of selective service, and visit medical advisory boards, local boards and examining physicians to advise and assist all concerned with physical examinations. They will keep the necessary records and statistical analyses of the operation of the medical function of Selective Service within the state.

NATIONAL HEADQUARTERS

The National Selective Service Headquarters in Washington will contain a compact medical division, which will assist the director of Selective Service in the determination of policy on medical matters and have general direction and coordination of the medical functions through the state headquarters and the medical assistants in each state.

INTANGIBLE BENEFITS OF SELECTIVE SERVICE

The training and service of hundreds of thousands of young men of the nation during the coming years, the improvement in their physical condition resulting from good food, regular hours, supervised physical endeavor and healthful environment, as well as a revival of that feeling of national unity which seems ever to be a part of a great national effort, will not be the only benefits which the nation will derive from Selective Service. There are certain other dividends which will be worth while. It is expected that the analyses of the reports of physical examinations and other records of Selective Service will make available many new data of sociological and medical importance. The occurrence of disease and disability as to character, locality, age group, color and nativity will give us a new measuring stick by which to judge the efficacy of the many and varied health programs that we have carried on in the last twenty years and will assist in the preparation of new plans for the future. These analyses will further disclose the physical fitness of the new generation and provide us with a current and more accurate measure of the available manpower of the country against "The Day" we pray may never come.

NEW NAVAL MEDICAL OFFICERS

The following candidates have been appointed assistant surgeons of the U. S. Navy with the rank of lieutenant (junior grade) to rank from July 15:

John W. Thomas, Phoenix, Ariz.
Charles J. Allen, Milwaukee.
Milo A. Youel, Minneapolis.
Alfred E. Cronkite, Los Angeles.
Vernon W. H. Campbell, Upper Darby, Pa.
George M. Davis, Bixby, Okla.
Rodney D. Chamberlain, Denver.
Thomas C. Ryan, Buffalo.
Charles G. Butler, Los Angeles.
John W. Flaiz, Vista, Calif.
Lloyd B. Kingsbery, Los Angeles.
Hardy Ulm, Atlanta, Ga.
Thomas L. Greason, Edgewood, R. I.
James H. Abernethy, Altus, Okla.
John F. Roach, Jamaica Plain, Mass.
Paul T. Moore, Milton, Mass.
Vinton Hall, Berkeley, Calif.
John W. Derbyshire, Madison, Wis.
Owen J. Deuby, Detroit.
Herschel E. Richardson, Nashville, Tenn.
Harry F. Lenhardt, Philadelphia.
David C. Stoner, Gettysburg, Pa.
Neville C. Bowers, Washington, D. C.
Melville M. Driskell, Atlanta, Ga.
Samuel S. Spicer, Madison, Wis.
Frank T. Norris, Wake Forest, N. C.
George H. Moseley, Metropolis, Ill.
Henry T. Gannon, Corning, N. Y.
Simon W. Eyer, Felton, Del.
Paul D. Hurley, Jamaica Plain, Mass.
John J. Head, Glen Rock, N. J.
John F. Shronts, Woodstock, Ill.
John E. Gorman, Wausau, Wis.
David P. Hightower, York, Ala.
Richard B. Williams Jr., Charlottesville, Va.
James G. Kurfees, Raleigh, N. C.
Lester M. Fox, Woodhaven, L. I., N. Y.
Vayle S. Briden, Merced, Calif.
Raymond W. Owens, Los Angeles.
James H. Higgins, Adrian, Mich.
Robert A. Welch, Salt Lake City.
Richard B. Brodrick, Philadelphia.
Deane S. Marcy, Hay Springs, Neb.
Mark R. Rhea, Arlington, Neb.
Bernard G. Geuting, Hamburg, N. Y.
Charles F. Hudson, Richmond, Va.
Jesse H. Suitor, Memphis, Tenn.
Leonard A. Becker, Chicago.

OHIO COMMITTEE MEETS

The committee on medical preparedness of the Ohio State Medical Association held a meeting at the association headquarters in Columbus, August 18, with seven of twelve members present in addition to the chairman, Dr. H. V. Paryzek, Cleveland. Dr. Fred W. Rankin, Lexington, Ky., member of the national committee for the Fifth Corps Area, attended the meeting. Plans were made to urge all physicians to complete and return the questionnaire of the American Medical Association and to request county societies to appoint preparedness committees. At the request of Governor Bricker, the committee discussed medical factors which would be involved in the selection of draft boards and submitted recommendations for his consideration.

ORGANIZATION SECTION

WOMAN'S AUXILIARY

Georgia

The executive board of the woman's auxiliary to the Medical Association of Georgia met in Atlanta with the advisory committee from the association, the latter group approving the year's projected work for the auxiliary at this time. Dr. James N. Brawner, of Atlanta, chairman of the advisory committee, presided over the meeting. Mrs. H. G. Banister, of Ila, recently installed president of the auxiliary, presented an outline of the work to be undertaken during the year. It was decided to sponsor the writing of health plays, and Dr. Brawner offered a prize of $10 for the best play submitted.

Utah

Mrs. E. L. Van Aelstyn discussed "What the Law Expects of the Physician" and presented the plan of the Utah Medical and Hospital Benefit Association at the March meeting of the auxiliary to the Carbon County Medical Society in Price.

The auxiliary to the Salt Lake County Medical Society has placed *Hygeia* in all the hospitals in Salt Lake City. Mrs. John Z. Brown, president of the auxiliary, presided at the recent meeting when the statue of "Hygeia," which was won as a prize by the auxiliary in the recent Hygeia Contest, was unveiled.

Dr. George Fister and Mr. W. M. Tibballs discussed the plan of the Utah Medical and Hospital Insurance before public meetings under the auspices of the auxiliary to the Utah County Medical Society in Provo recently.

At the February meeting of the auxiliary to the Weber County Medical Society in Ogden, Mrs. Claude L. Shields spoke on "Budgeting Your Time."

Virginia and West Virginia

The woman's auxiliaries to the West Virginia and Virginia medical associations held a joint annual meeting in White Sulphur Springs, W. Va., July 29-31. Mrs. V. E. Holcombe, president of West Virginia auxiliary, also national president, and Mrs. H. A. Latane, president of the Virginia auxiliary, presided over the business meetings of their respective auxiliaries. There were 114 registered from West Virginia and 119 from Virginia.

On West Virginia Day a luncheon was given for both auxiliaries, with Mrs. Holcombe acting as hostess to about thirty distinguished guests at the speakers' table and 200 auxiliary members. Dr. Hugh Trout, president of the Medical Society of Virginia, and Dr. Frank Longfitt, president of the West Virginia State Medical Association, were among the honored guests. The principal address was given by Mrs. Charles P. Corn, president of the Southern medical auxiliary.

At the annual election of officers for the two states, Mrs. H. V. Thomas took office as president of the West Virginia auxiliary and Mrs. Griffin W. Holland as president of the Virginia auxiliary.

At the annual dinner Governor and Mrs James Price of Virginia and Governor and Mrs. Frank Holt of West Virginia were present. Both governors gave short addresses.

MEDICAL ECONOMIC ABSTRACTS

MEDICAL CARE IN GEORGIA

After making a thorough study of medical facilities and needs throughout the state, the Medical Association of Georgia conducted a symposium on the Problems of Medical Care in Georgia in Savannah, April 24.[1] The statistical study which laid the factual basis of the symposium included a complete survey of the state to determine "the total population per county serviced by one physician, the number of whites per county serviced by one physician, and the square miles covered by one physician per county. These statistics were correlated with the net taxable values per county." This study was conducted by Dr. Alfred A. Weinstein and Dr. C. W. Roberts from the Emory University School of Medicine.

It was found that there was a fairly close correlation between the county taxable values and the number of physicians in the county. "The two extremes were as follows: Chattahoochee County with net taxable values of $250,630 had no physicians; Fulton County with net taxable values of $229,775,695 had 653 physicians." When this correlation was graphed it became evident that the "number of physicians in a county begins to rise sharply only after the net taxable values in the county increase over $2,000,000."

There has been a positive decrease of 144 in the number of physicians in Georgia in the years from 1931 to 1936. This decrease has been largely in the low income rural areas where there were already the fewest physicians. "There were 2,285 physicians engaged in general practice in Georgia in 1938. In the rural areas there is one physician per 1,800 population, in the urban areas 1 : 1,000, and for the state as a whole 1 : 1,560. In the United States the ratio was 1 : 785." It is suggested "that certain counties may see fit to partially subsidize a practitioner to care for the medically indigent, and simultaneously permit him to carry on private practice among those who can afford to pay."

A study of the distribution of hospitals showed that Georgia has a lower ratio of hospital beds per population than most of the states. This is largely due to the low incomes which prevail. Some estimates have fixed the per capita income in Georgia as low as $146 annually. Dr. T. F. Abercrombie, director of the Georgia Department of Public Health, recognizes that any widespread distribution of hospitals is liable to overlook maintenance costs and expect to obtain these from pay patients. Group hospitalization, while it has proved helpful, does not meet all emergencies. "During an influenza epidemic" in Atlanta "when hospitals were overflowing because people who had paid their hospitalization fee demanded benefits whether hospital care was necessary or not it was almost impossible to get emergency cases admitted." He also finds that malnutrition is an extremely serious problem and that "If the whole population were adequately nourished our public health and medical care programs would be simplified immensely."

There was considerable discussion of hospital programs and plans for the care of the indigent. The discussion of hospital planning was based on illustrations from several counties that had recently constructed hospitals largely under the direction of the county medical society. The problem of adequately staffing these is still an important one. Prepayment plans under the direction of organized medicine were suggested in accordance with the resolutions adopted by the House of Delegates of the American Medical Association.

It was pointed out that education of individuals on the necessity of seeking good medical care and avoiding self diagnosis and self treatment through "patent medicines" and patronage of quacks is of paramount importance.

1. Symposium on the Problems of Medical Care in Georgia, J. M. A. Georgia **29**: 341 (July) 1940.

THE GENERAL PRACTITIONER AND HIS HANDBAG

(From the *North Carolina Medical Journal*, June 1940)

In his recent book The Patient's Dilemma, Dr. Hugh Cabot quotes the following statement from Dr. Morris Fishbein: "Obviously, 85 per cent of the diseases for which patients consult doctors are of the type which the general practitioner can handle with the amount of equipment that he can carry in a handbag." Dr. Cabot's comment is "We shall, I think, be on sound ground in asserting that this statement never was true and that it is even less true today. . . . I am unaware of any evidence . . . acceptable to any scientific body which would support Dr. Fishbein's allegation."

In an effort to find out which of these views was correct, five Winston-Salem medical men tabulated an average of 200 consecutive cases each. Of the 1,000 patients thus reviewed 848, or 84.8 per cent, had been cared for without any other equipment than the contents of a handbag. A modern doctor's handbag, be it remembered, contains at least a blood pressure apparatus, a stethoscope, a hypodermic syringe, an otoscope, an ophthalmoscope, a transillumination light, a blood counting apparatus, glass slides, a hemoglobin scale, a pleximeter, tongue depressors, Wassermann tubes, culture tubes, and a few other odds and ends.

In tabulating these cases, every patient who had to have a basal metabolism reading, an x-ray examination, an electrocardiogram, an operation or a surgical consultation or who was referred to a clinic for a diagnostic survey was included in the referred group even if the doctor had his own basal metabolism apparatus or electrocardiograph. A considerable number of these referred patients, it should be noted, were beyond real help from any medical source: for example, some with arthritis, some with incurable mental disease, and a few who literally enjoyed poor health too much to exchange it for an active existence.

The lowest proportion of patients cared for unaided by an individual doctor was 82 per cent, the highest 89 per cent. The average of 84.8 per cent is certainly close enough to 85 to be acceptable to most scientific bodies as supporting Dr. Fishbein's statement.

MEDICAL SERVICE ASSOCIATION ORGANIZES

At a meeting of the members of the Medical Service Association of Pennsylvania, held on April 3, 1940, in Harrisburg, the amendments to the by-laws of the association suggested by action of the house of delegates at its special meeting held Feb. 28, 1940, were adopted. The following members were in attendance: Louis H. Clerf, Walter F. Donaldson, Chauncey L. Palmer, Lester H. Perry, David W. Thomas, A. Alfred Wasserman and G. Harlan Wells. Robert L. Anderson and Robert V. White were absent on account of illness.

Immediately following the membership meeting a meeting of the board of directors was held at which the following officers were elected: president, Chauncey L. Palmer, Pittsburgh; first vice president, Louis H. Clerf, Philadelphia; secretary, Lester H. Perry, Harrisburg; treasurer, Robert L. Anderson, Pittsburgh; members of executive committee, Walter F. Donaldson, Pittsburgh, David W. Thomas, Lock Haven, Dr. Palmer, and Mr. Perry.

Three problems were referred to the Executive Committee: (1) The problem of alternative plans on the deductible or limited service principle; (2) the problem of the maximum benefits allowed in any one year, and (3) the wording of the section in the Participating Physician's Agreement to cover the $3 assessment.

At the present time the executive committee is working on these three problems with the objective that within the very near future the entire plan in its revised form will be presented to the state insurance commissioner for his approval.

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

Personal.—Dr. John B. Plum, Nashville, Tenn., has been appointed to the staff of the state department of health, succeeding Dr. Charles J. Westover, Anniston, as tuberculosis clinician. The latter has resigned to enter private practice in Michigan, newspapers reported.

Society News.—Drs. James A. Becton, Birmingham, and Merle E. Smith, Parrish, addressed the Walker County Medical Society, Jasper, August 9, on "Shock in the Treatment of Certain Mental Diseases" and "The Sulfonamides in Therapy" respectively. Dr. James R. Garber, Birmingham, discussed problems in obstetrics before the society recently.

Medical Seminar.—The Jefferson County Medical Society sponsored a seminar in Birmingham, September 16-17. Among the speakers were Drs. Marion Arthur Blankenhorn, Cincinnati; Francis Bayard Carter, Durham, N. C.; George Argale Harrop, Princeton, N. J.; Willis D. Gatch, Indianapolis; William Wirt Waddell Jr., Charlottesville, Va., and John Albert Key, St. Louis.

ARKANSAS

Personal.—Dr. Louis K. Hundley, Warren, formerly health director of Bradley County, has been assigned to the trachoma control service of the state board of health.

Changes in Health Officers.—Dr. Albert W. Thompson, Bentonville, has been appointed medical director of the Benton County health unit, succeeding Dr. James B. Tucker, resigned. ——Dr. Neil E. Compton, Warren, has been appointed director of the Bradley County health unit.——Dr. Raymond E. Smallwood, Little Rock, has been named in charge of the Garland County health unit.

CALIFORNIA

Long Incubation Period in Rabies.—An incubation period of 113 days for rabies was recently reported for a dog in San Francisco, the longest incubation period recorded in the city's history of the disease. According to the health department, this is important in view of the fact that the ordinary quarantine period in California for any dog bitten by a rabid dog is three months. On April 16 a pet dog was bitten by a stray dog. The latter died a few days later of rabies confirmed on microscopic examination of the brain. The pet dog showed a slight wound on the left hind leg and was taken to the public pound, April 19, where it remained in solitary confinement until July 19. Physical examination of this animal on release gave negative results. It is positively stated that it had not come in contact with other dogs. Later in July the animal was returned twice to the pound for clipping and bathing. On August 3 the dog was admitted to a private veterinary hospital because of illness which became gradually worse, and it died August 6 of rabies confirmed by microscopic examination of the brain. In the interval from July 19, when it was released from the pound, to August 3, when the animal became ill, the dog did not come in contact with other animals, having been confined on its owner's premises with the exception of the two return visits to the pound, it was stated. Up to May 15, 1939, when a positive examination for animal rabies was reported, San Francisco had been free from this disease for many years. Since that time there have been sixty-six cases.

DISTRICT OF COLUMBIA

Emergency Facilities.—A booklet has been compiled by the Health Security Administration, Washington, entitled "Emergency Facilities." It is a directory of information on hospitals and ambulances, with particular reference to their locations and methods of immediate contact, and covers the emergency facilities in Washington, nearby Maryland and Virginia. Telephone numbers are listed and various services are classified, making the general information available to the public at large and acting as a time-saver to telephone operators, personnel of police departments, fire departments, hospitals, private physicians and nurses, ambulance attendants and others. The booklet is available on request to the Health Security Administration, Health Security Center, 1823 L Street, N.W., Washington.

FLORIDA

Personal.—Dr. Lamar L. Lancaster, Lake Wales, has been appointed superintendent of the Polk County Hospital, Bartow, succeeding Dr. Julian L. Hargrove. The latter resigned after fifteen years' service to take over the city hospital on a dollar a year lease basis, newspapers reported.

Annual Regional Meetings.—The fourth annual meeting of the Northeast Medical District of the Florida Medical Association will be held at the Ocean Dunes Club, Daytona Beach, October 3, with the following speakers, among others:

Dr. George M. Green, Daytona Beach, Amnesia and Short Labor.
Dr. Theodore F. Hahn, DeLand, Staphylococcus Toxoid.
Dr. John W. Snyder, Miami, The Splenomegalias with Surgical Indications.

At the fourth annual meeting of the North Central Medical District in the Blanche Hotel, October 4, Lake City, the speakers will include:

Dr. Thomas H. Wallis, Ocala, Use of Endocrines in Treatment of Functional Menstrual Disorders.
Dr. William C. Thomas, Gainesville, A Review of 550 Consecutive Cases of Pregnancy with Hospital Delivery.
Dr. Councill C. Rudolph, St. Petersburg, Roseola Infantum.

The fourth annual meeting of the Northwest Medical District at the San Carlos Hotel, Pensacola, October 5, will be addressed by the following, among others:

Dr. James H. Pound, Tallahassee, Case Report of Staphylococcus Septicemia Treated with Sulfathiazole.
Dr. Rayburn N. Joyner, Marianna, Pectin in the Treatment of Chronic Ulcers.
Dr. William H. McCullagh, Jacksonville, Treatment of Some of the Common Neuropsychiatric Disorders.

ILLINOIS

Society News.—Eldridge T. McSwain, Ed.D., associate professor of education, Northwestern University, Evanston, addressed the Peoria City Medical Society in Peoria, September 10, on "Education's Contribution to Adolescence in a Democracy."——The Sangamon County Medical Society was addressed in Springfield, September 5, by Dr. Carl-Gustaf D. Tillman, Topeka, Kan., on "Medical Aspects of Chronic Alcohol Addiction."

Free Laboratory Diagnostic Service.—A limited laboratory service in the diagnosis of cancer is now available from the state department of public health to the physicians of Illinois. Biopsy specimens taken from poor patients will be accepted and examined free at the department's diagnostic laboratories in Chicago. Specimens taken from patients able to pay for such service should be sent to privately operated pathologic laboratories. Physicians and dentists who use this service are urged to select the specimens for biopsy with great care. The specimen should be large enough to include the lesion and also, if possible, a small part of adjacent normal tissue. It should be removed without crushing, placed immediately into a 10 per cent solution of formaldehyde and mailed in a tightly sealed container to the Cancer Diagnostic Service, State Department of Public Health, 1800 West Fillmore Street, Chicago. These specimens should be taken only when there are reasonable grounds for suspecting tumors. Reports of examinations will be placed in the mails usually within forty-eight hours after receipt of specimens. While this service is now limited practically to the laboratory examination of specimens submitted, it is anticipated that later the service can provide a source of material for those interested in tumor pathology and will serve as a medium for the exchange of impartial and friendly views on the diagnosis of tumor material. Dentists and oral surgeons are also invited to use the service. The diagnostic service will work in cooperation with the recently established division of cancer control, the work of which is educational in character. With Dr. Perry J. Melnick in charge, the cancer diagnostic service is a unit in the division of laboratories. Dr. Raymond V. Brokaw is chief of the division of cancer control, an administrative unit of the state department of public health.

Chicago

Society News.—The North Side Branch of the Chicago Medical Society will be addressed, October 3, by Dr. Elliott C. Cutler, Boston, on "The Art of Surgery."

University News.—Charles W. Patterson, Ph.C., registrar of Northwestern University Medical School for twenty-seven years, has been retired with the title associate professor emeritus of pharmacology. He had been associated with the school for forty-seven years.——The medical department of the University of Chicago eventually will receive all of the estimated $100,000 estate of the late William S. Oppenheim. Under a trust established by the will, the income will go to relatives during their lifetime. The entire residuary estate is left to the university.

IOWA

Personal.—Dr. Albert J. Entringer, in charge of the Dubuque health department, has been appointed a member of the faculty of Loras College, effective September 1; he will lecture on health and hygiene to freshman students.——Dr. Thomas P. Bond, Des Moines, was recently granted life membership in the Polk County Medical Society; he has been a life member of the state medical society for the past three years.——Dr. Harry H. Ennis, LeMars, formerly medical director of district number 1, has been placed in charge of the Northeastern Iowa health unit with offices in Decorah.

Infantile Paralysis in Iowa.—The peak is believed to have been reached in the spread of poliomyelitis in Iowa, newspapers reported September 21. Of 400 cases reported since last spring, 176 were recorded in August and 200 up to September 21. It was estimated that at the time of this report 350 cases were still active. According to the newspapers, the disease was spread fairly evenly over the state, eighty of the ninety-nine counties having one or more cases. However, there were a few definite centers, the city of Waterloo being the hardest hit. Other concentrations were at Sioux City and in the counties of Appanoose and Bremer. All public social activities in Waterloo have been discouraged for several weeks. The opening of the schools was delayed three weeks but was expected to take place September 23. Children were refused admission to theaters, and such gathering places as swimming pools and clubs were closed.

Postgraduate Programs in Des Moines.—The Polk County Medical Society opened a series of postgraduate programs in Des Moines, September 18, with Drs. James T. Priestley, Rochester, Minn., and Clifford J. Barborka, Chicago, as the speakers. Their subjects were, respectively, acute conditions of the abdomen and "Food in the Practice of Medicine." Subsequent programs will be:

October 16: Drs. Addison W. Brown and Lindsay J. Ervin, Des Moines, Carcinoma of the Cervix and Drip Method in Treatment of Syphilis, respectively.
November 20: Drs. James Barrett Brown, St. Louis, and Andrew C. Ivy, Chicago, Traumatic Surgery and Relation of Physiology to Modern Medicine, respectively.
December 18: Dr. Julius S. Weingart, Des Moines, A Short Pathologic Conference.
March 19: Drs. David P. Barr, St. Louis, and George E. Shambaugh Jr., Chicago, The Making of a Diagnosis of Head Infections in Relation to General Practice, respectively.
February 19: Drs. Howard D. Gray, Avoidable Errors in Technic in Surgery of the Female Pelvis; Clifford W. Losh, Some Practical Points of Urology for the General Practitioner; Walter D. Abbott, Surgical Treatment of Intractable Pain, and Dwight C. Wirtz, Treatment of Tendon Injuries. All are of Des Moines.
May 21: Drs. Elmer L. Sevringhaus, Madison, Wis., and Eugene M. K. Geiling, Chicago, Endocrinology in General Practice and New Drugs, respectively.
April 16: Drs. Richard F. Birge, Des Moines, and Franklin E. Walton, St. Louis, Symposium on the Thyroid.

LOUISIANA

New Professor of Ophthalmology.—Dr. William Burton Clark, associate professor of ophthalmology, Tulane University of Louisiana School of Medicine, New Orleans, has been appointed professor, effective September 1. He succeeds Dr. Wiley R. Buffington, who has retired to devote his full time to private practice. Dr. Clark graduated at Emory University School of Medicine, Atlanta, Ga., in 1927 and has been associated with the faculty at Tulane since 1933.

Personal.—Dr. Edgar Galloway, Vivian, has been chosen superintendent of the Charity Hospital, Shreveport, succeeding Dr. Edgar L. Sanderson, who held the position for twelve years.——Dr. Marion H. Foster, Alexandria, has been appointed superintendent of the Huey P. Long State Charity Hospital, Pineville, succeeding Dr. Osmyn W. McFarland, resigned.——Dr. Edgar Hull, clinical professor and head of the department of medicine, Louisiana State University Medical Center, New Orleans, has been granted a leave of absence from October 15 to May 15 of next year to accept a temporary appointment as associate professor of medicine at Yale University School of Medicine, New Haven.

MARYLAND

Changes in Health Officers.—Dr. Josiah S. Bowen, head of the Baltimore County Health Department for twenty-six years, has resigned, newspapers reported recently. Dr. William H. F. Warthen, assistant health commissioner of Baltimore for the past six years, has been appointed to succeed Dr. Bowen.——Dr. Ralph F. Sikes, formerly with the Connecticut state health department, has been appointed senior medical supervisor in the bureau of venereal diseases in the Baltimore City Health Department.

MASSACHUSETTS

Dr. Packard Named Director of Biological Laboratory.—Charles Packard, Ph.D., of the Institute of Cancer Research, Columbia University, New York, has been appointed director of the Marine Biological Laboratory, Woods Hole. He had been assistant director since 1938 and previously had been clerk of the corporation for seven years. Dr. Packard has been at the Institute of Cancer Research since 1924. He took his doctorate in philosophy at Columbia in 1914.

Institute on Science and Food.—Wellesley College, Wellesley, will hold an institute on science and the nation's food, October 24-26, to bring together nationally recognized experts for discussion, to give undergraduates a sense of "the social outreach of their laboratory discipline" and to emphasize the role of the college as an "agency of scientifically implemented culture" working to advance the common good. The departments of botany, chemistry, economics, geography, hygiene and physiology are cooperating under the direction of Ruth Johnstin, Ph.D., of the chemistry faculty.

MICHIGAN

Changes in Health Officers.—Dr. Richard Sears, Fremont, director of the tri-county health unit composed of Newaygo, Oceana and Lake counties since October 1938, has been named director of the Muskegon County health department, succeeding Dr. Reuben J. Harrington.

Appointments at Wayne.—Dr. Carl C. Pfeiffer, formerly of Chicago, has been placed in charge of a new branch of toxicology and will supervise the pharmacodynamic work in the Wayne University College of Pharmacy, Detroit. Paul S. Larson, Ph.D., formerly instructor in physiology at Georgetown University School of Medicine, Washington, D. C., has been appointed lecturer in the department of pharmacology. Dr. Pfeiffer graduated at the Department of Medicine, University of Chicago, in 1937. Dr. Larson received his degree as doctor of philosophy at the University of California in 1934.

Infantile Paralysis.—Fifty-eight counties in Michigan have reported cases of poliomyelitis in September, recording a total of 200 more than for the same period in 1939, according to a release from the state department of health, September 23. Accounting for 298 cases, twenty-four counties reporting five or more cases of the disease through September 18 are: Alger ten, Allegan five, Barry thirteen, Berrien seven, Branch nine, Calhoun eight, Delta ten, Dickinson thirteen, Eaton five, Gogebic seven, Ingham twenty-nine, Iron ten, Kalamazoo fourteen, Kent forty-three, Luce thirty-one, Mackinac five, Mecosta five, Midland six, Muskegon eight, Ottawa five, St. Joseph eight, Van Buren eleven, Washtenaw five and Wayne thirty-one. Sixty cases had been reported in September to the time of this report in thirty-four other counties.

New President and Director of Kellogg Foundation.—George B. Darling, Dr.P.H., associate director, and Emory W. Morris, D.D.S., associate executive director of the W. K. Kellogg Foundation, Battle Creek, were elected president and general director, respectively, August 19, succeeding the late Dr. Stuart Pritchard, who held both positions. Dr. Darling and Dr. Morris have been associated with the foundation for many years. Both received their degrees at the University of Michigan. The foundation has announced that it would spend $2,553,650 in the coming year to further the health and well-being of children. All but $634,000 will be spent in the counties of Calhoun, Allegan, Van Buren, Barry, Branch, Eaton and Hillsdale, where the foundation conducts community health projects. The $634,000 will be expended as grants to various institutions.

MINNESOTA

Personal.—Dr. Richard B. Girvin has been appointed Minneapolis medical examiner for the Civil Aeronautics Authority, succeeding Dr. Albert J. Herbolsheimer, who has gone to Washington, D. C., with the authority.——Dr. Marcus H. Flinter, head of the Cass Lake Indian Hospital, Cass Lake, has been transferred to Arizona, where he will be in charge of an Indian tuberculosis sanatorium at Phoenix, according to *Minnesota Medicine*.

NEW JERSEY

Personal.—Robert P. Fischelis, Phar.D., secretary and chief chemist of the Board of Pharmacy of the State of New Jersey, has been appointed a member of the American Council on Pharmaceutical Education as one of three representatives of the American Pharmaceutical Association. The council is the accrediting agency for colleges of pharmacy. Dr. Fischelis will serve six years.

Society News.—Dr. James T. Rugh, Philadelphia, addressed the Gloucester County Medical Society, Woodbury, September 19, on "Low Back Pain—Causes and Treatment."——Dr. Arthur C. DeGraff, New York, will address a stated meeting of the Academy of Medicine of Northern New Jersey, Newark, October 17, on "The Present Status of Digitalis Therapy."——Dr. Frank W. Konzelmann, Philadelphia, addressed the Atlantic County Medical Society, Atlantic City, September 13, on "Biochemistry of Disease."——Dr. Jay Arthur Myers, Minneapolis, will address the Bergen County Medical Society, October 8, at Bergen Pines, on "Follow-Up Work in Tuberculin Testing Surveys."

NEW YORK

District Meetings.—The Fifth District Branch of the Medical Society of the State of New York held its annual meeting at Little Falls, September 24, with the following program:

Dr. Harry Dan Vickers, Little Falls, Newer Concepts of Hypertension.
Dr. George G. Ornstein, New York, Diagnosis of Carcinoma of the Lung.
Dr. Brewster C. Doust, Syracuse, Appendicitis in Children.
Dr. John C. A. Gerster, New York, General and Local Crymotherapy.
Dr. Henry Van Zile Hyde, Syracuse, Chemotherapy.

The Seventh District Branch held its annual meeting at the Clifton Springs Sanitarium, Clifton Springs, September 26. Drs. Herbert F. Dyer, Hamilton, Ont., and Elmer Milch, Buffalo, spoke on "Recognition and Prevention of the Late Toxemias of Pregnancy in Their Incipient Stages" and "Treatment of General Peritonitis Following Ruptured Appendix" respectively. The following officers of the state society made brief talks: Drs. James M. Flynn, Rochester, president; Peter Irving, New York, secretary; Joseph S. Lawrence, Albany, executive officer, and Mr. Dwight Anderson, New York, publicity director. A medical "correct or incorrect" contest was held, with Dr. Floyd S. Winslow, Rochester, as master of ceremonies.

New York City

Personal.—Dr. Russell L. Cecil has been made an honorary member of the Argentine League Against Rheumatism, according to *New York Medical Week*.——Dr. Israel S. Wechsler was appointed a member of the medical board of Hadassah, the Women's Zionist Organization of America, in addition to those reported in THE JOURNAL, August 3, page 395.

Tuberculosis Conference.—The Tuberculosis Sanatorium Conference of Metropolitan New York will hold a clinical session at Cornell University Medical College, October 9. The speakers will be Drs. Samuel Cohen, Jersey City, on lymphohematogenous tuberculosis and Oscar Auerbach, Staten Island, extrapulmonary tuberculosis. Dr. Mather Cleveland will present a discussion of "Joint Tuberculosis" and Dr. Howard S. Jeck, "Genito-Urinary Tuberculosis." Dr. Grant Thorburn will preside.

Friday Afternoon Lectures in Brooklyn.—The Medical Society of the County of Kings and Academy of Medicine of Brooklyn will open their series of Friday afternoon lectures October 4, with Dr. A. Benson Cannon as the speaker on "Diagnostic and Therapeutic Aspects of Dermatological Diseases." Other speakers for October will be:

Dr. George G. Ornstein, Clinical Aspects and Recent Contributions to the Treatment of Pulmonary Tuberculosis, October 11.
Dr. James M. Tarsy, Regional and Local Analgesic Injections for Local and Intractable Pain, October 18.
Dr. Samuel L. Siegler, Diagnostic and Therapeutic Aspects of Sterility, October 25.

NORTH CAROLINA

Diseases of Metabolism and of Blood-Forming Organs.—Duke University School of Medicine and Duke Hospital, Durham, will present a symposium, October 31 to November 2, on diseases of metabolism and of the blood-forming organs. The speakers will be:

Dr. Cyrus C. Sturgis, Ann Arbor, Mich., Hemorrhagic Diseases.
Dr. Louis K. Diamond, Boston, Practical Aspects of Treatment of Anemias in Childhood.
Dr. Claude E. Forkner, New York, The Leukemias.
Dr. Elliott P. Joslin, Boston, Diabetes and Its Treatment.
Dr. Thomas B. Cooley, Detroit, Hemolytic Anemias.
Dr. Fuller Albright, Boston, The Diagnosis of Hyperparathyroidism.
Dr. Eugene F. DuBois, New York, Clinical Application and Interpretation of the Basal Metabolic Rate.
Dr. Frank H. Lahey, Boston, President-Elect of the American Medical Association, Management of Hyperthyroidism; also A Practical Discussion of Surgical Diseases of the Thyroid Exclusive of Hyperthyroidism.
Dr. Allen O. Whipple, New York, Indications for and Results Following Splenectomy.
Dr. Leland S. McKittrick, Boston, Surgical Complications of Diabetes.
Dr. George R. Minot, Boston, Some Aspects of the Etiology, Diagnosis and Treatment of Iron Deficiency Anemias and Pernicious Anemia.
Dr. Frank A. Evans, Pittsburgh, The Nature of Obesity, Its Prevention and Cure.
Dr. Alexis F. Hartmann, St. Louis, The Complete Treatment of Diabetes Acidosis.
Dr. Russell M. Wilder, Rochester, Minn., What Is Hyperinsulinism?

OHIO

Personal. — Dr. Francis E. Mahla, Marion, has been appointed health officer of Sandusky and Erie County to succeed the late Dr. Frederick M. Houghtaling. Dr. Mahla was formerly assistant state health director.——Dr. Earl C. Van Horn, Oxford, has been appointed medical superintendent of the Ohio Masonic Home, Springfield.——Dr. Harry A. Neiswander, Pandora, has been appointed health commissioner of Putnam County, succeeding Dr. Louis M. Piatt, Ottawa, resigned.——Dr. Otto K. Engelke, West Union, has resigned as health officer of Adams County to join the Kellogg Foundation, Battle Creek, Mich.——Dr. Jonas L. Hurst, Dorset, has resigned as health officer of Ashtabula County.

Society News.—The semiannual meeting of the Ohio State Hospital Physicians' Association will be held at Longview State Hospital, Cincinnati, October 3-4. Among the speakers will be Drs. Douglas Goldman, Cincinnati, on "Electric Shock Therapy" and George H. Cook and John A. Dole Jr., Gallipolis, "Benzedrine Sulfate in Treatment of Epilepsy." Dr. Tom Douglas Spies, Cincinnati, will open a symposium on vitamin deficiencies and Dr. David A. Boyd Jr., professor of psychiatry, Indiana University School of Medicine, Indianapolis, will be the guest speaker at a banquet Thursday evening.—— Dr. Theodore P. Eberhard, medical director of the Ellis Fischel State Cancer Hospital, Columbia, Mo., addressed the Summit County Medical Society, Akron, September 3, on "Certain Phases of the Cancer Problem." —— Dr. Edgar V. Allen, Rochester, Minn., will address the Mahoning County Medical Society, Youngstown, October 22, on "Peripheral Circulation."

OKLAHOMA

Personal.—Dr. Woodrow L. Pickhardt, formerly of Chicago, has been appointed health officer of a new unit in Creek County with headquarters in Sapulpa.——Dr. Howe K. Riddle, Coweta, has been appointed health officer of Wagoner County, succeeding Dr. Walter R. Joblin, Porter.

Society News. — Dr. Ferdinand C. Helwig, Kansas City, Mo., addressed the Tulsa County Medical Society, Tulsa, September 23, on "Clinical and Experimental Studies of Coronary Disease with Special Emphasis on Trauma."——Drs. Carl S. McMurray, Nashville, Tenn., and Wann Langston, Oklahoma City, addressed the Southern Oklahoma Medical Association in Shawnee, September 26, on "Endocrine Considerations in Gynecology" and "Blood Dyscrasias" respectively.——Dr. Paul C. Gallaher, Shawnee, addressed the Pottawatomie County Medical Society, Shawnee, July 20, on rheumatic fever.

Annual Fall Clinical Conference.—The tenth annual fall clinical conference of the Oklahoma City Clinical Society will be held in Oklahoma City, October 28-31, at the Biltmore Hotel. Postgraduate courses, general assemblies, round table luncheons and evening symposiums will make up the program. Dr. Nathan B. Van Etten, New York, President of the American Medical Association, will be a special guest, and scientific speakers will include:

Dr. William B. Carrell, professor of orthopedic surgery, Baylor University College of Medicine, Dallas, Texas.
Dr. Robert J. Crossen, assistant professor of clinical obstetrics and gynecology, Washington University School of Medicine, St. Louis.
Dr. Elliott P. Joslin, clinical professor of medicine emeritus, Harvard Medical School, Boston.
Dr. Norman M. Keith, professor of medicine, University of Minnesota Graduate School, Rochester.
Dr. Joseph Earle Moore, associate in medicine, Johns Hopkins University School of Medicine, Baltimore.
Dr. Edmund B. Spaeth, associate professor of ophthalmology, University of Pennsylvania Graduate School of Medicine, Philadelphia.
Dr. A. Elmer Belt, associate professor of urology, College of Medical Evangelists, Los Angeles.
Dr. Morris Edward Davis, associate professor of obstetrics and gynecology, University of Chicago School of Medicine.

Information concerning the conference may be obtained by addressing the secretary, 512 Medical Arts Building, Oklahoma City.

OREGON

Personal.—Dr. Joseph F. Wood, Portland, has resigned as secretary of the state board of medical examiners and from membership on the board. Dr. Linford S. Besson, Portland, is acting secretary.——Dr. Keith P. Russell, Portland, has been appointed director of the division of communicable disease control in the city department of health.

Counties Sponsor Postgraduate Course.—The postgraduate committee of the Polk-Yamhill-Marion Counties Medical Society will sponsor a postgraduate symposium on gastrointestinal diseases by the following members of the faculty of the University of California Medical School, San Francisco: Drs. Montague S. Woolf, Felix Cunha and Fred H. Kruse. The meetings will be in Salem, October 10-11. There will be a registration fee of $5.

PENNSYLVANIA

Society News.—Dr. Carl J. Wiggers, Cleveland, addressed the Washington County Medical Society, Washington, September 11, on "The Problem of Ventricular Fibrillation and Cardiac Resuscitation."——Drs. Henry T. Price and Theodore O. Elterich, Pittsburgh, addressed the Westmoreland County Medical Society, Greensburg, September 17, on "Care of the Newborn" and "Convulsions in Childhood" respectively. —— Dr. Eldridge L. Eliason, Philadelphia, addressed the Cambria County Medical Society, Johnstown, September 12, on "The Patient and His Fracture."——Dr. Harvey G. Beck, Baltimore, addressed the Lawrence County Medical Society, New Castle, September 5, on "Chronic Illness Resulting from Carbon Monoxide."

GENERAL

Airplane Accidents.—The *Statistical Bulletin* of the Metropolitan Life Insurance Company in its August issue reports that in 1938 deaths resulting from all types of aviation activities, civil and military, numbered 436. Fatalities of this kind were 214 in 1927, 473 in 1928 and 596 in 1930. A decline took place in 1931 to 490 deaths. It is pointed out that one reason why the expected rise in fatalities did not materialize is that the anticipated increase in operation of privately owned planes did not take place.

Association for Advancement of Oral Diagnosis.—The American Association for the Advancement of Oral Diagnosis, established in 1938, will hold its annual meeting at the New York Academy of Medicine, October 17-18, during the annual Graduate Fortnight of the Academy. The purposes of this organization are to correlate oral diagnosis in dentistry and medicine, to encourage the biological, scientific and professional aspects of dentistry, and to foster cooperative research. Physicians and dentists of the organized medical and dental professions who are members in good standing in their respective organizations in the counties in which they practice are eligible for membership. Information may be obtained from H. Justin Ross, D.D.S., 515 Madison Avenue, New York.

Association of Military Surgeons. — The forty-eighth annual meeting of the Association of Military Surgeons of the United States will be held at the Hotel Statler, Cleveland, October 10-12, under the presidency of Major Gen. Charles R. Reynolds, U. S. Army, Ret. Among the speakers will be:

Rear Admiral Ross T. McIntire, Surgeon General, U. S. Navy, Selection of Men Adapted for Special Fields.
Dr. Crawford N. Baganz, Lyons, N. J., So-Called Shell Shock: Types, Etiology and Means for Its Prevention.
Dr. Russell L. Haden, Cleveland, Chemotherapeutic Developments Since the Last War.
Capt. Douglas B. Kendrick Jr., M.C., U. S. Army, Washington, D. C., Preparation, Supply, Distribution and Use of Blood Plasma in Military Service as Determined by the Committee Working with the Research Committee of the National Defense Council.
Drs. Ernest P. McCullagh and George Crile, Cleveland, Differential Diagnosis of Neurocirculatory Asthenia (Soldier's Heart) and Results in 152 Denervations of the Adrenal Glands in Treatment of Neurocirculatory Asthenia.
Lieut. Albert R. Behnke, U. S. Navy, Washington, D. C., Submarine Problems.
Dr. Gustavus M. Blech, Chicago, Surgical Technic in Modern Battle.
Brig. Gen. Frank T. Hines, Administrator of Veterans' Affairs, Washington, D. C., The Veterans' Administration and National Defense.

Committee Studies Antimalarials. — A committee on chemotherapy appointed by the National Research Council to stimulate research on new and useful synthetic drugs has begun its work with antimalarials as its first assignment. The committee was formed as a permanent organization after the group, appointed on a temporary basis by the division of chemistry and chemical technology, had made a preliminary survey of the field of malaria and antimalarials. Its original objective was the study of malaria, in view of the possibility that the supply of quinine from Java may be cut off and because the synthetic drugs are more expensive than many can afford, it was said. After the survey it was felt that the committee should concern itself not solely with antimalarials but should have as its function chemistry in the service of medicine. The broader field will permit the committee to offer its services to combat other diseases as well. The chairman of the committee is Marston T. Bogert, Ph.D., professor emeritus of organic chemistry at Columbia University, and the members are Lyndon F. Small, Ph.D., of the National Institute of Health, Washington, D. C.; Leonard H. Cretcher, Ph.D., assistant director of Mellon Institute, Pittsburgh; Dr.

Lowell T. Coggeshall, of the International Health Division of the Rockefeller Foundation, New York, and Dr. Torald H. Sollmann, dean, Western Reserve University School of Medicine, Cleveland. The committee has as one of its objects a closer cooperation between pharmacologists and chemists. It plans to function as a clearing house for information as to the chemists, manufacturers, pharmacologists and others now at work in the field, the special lines of investigation they are following and any other pertinent data. Preparation of a compact semipopular presentation of the malaria situation throughout the world, and particularly in this country, including a summary of what is being done here and how it is being handicapped and retarded by lack of funds, is another plan. Funds will be sought to support the committee's work, to establish research fellowships and to finance other activities that will advance achievement of its objects. Finally, the committee asks that individuals, organizations, institutions and manufacturers who are willing to cooperate communicate with Dr. Bogert at Havemeyer Hall, Columbia University, New York.

Pan American Congress of Ophthalmology.—The first Pan American Congress of Ophthalmology, sponsored by the American Academy of Ophthalmology and Otolaryngology, will be held in Cleveland, October 11-12, immediately after the annual meeting of the Academy. Among speakers announced for the program are:

Dr. Manuel U. Troncoso, New York, The Value of Gonioscopy in the Prognosis and Treatment of Glaucoma.
Dr. Manuel Marquez y Rodriguez, Mexico City, The Best and Most Exact Method for Diagnosis of Slight Astigmatism by Means of Bicylindrical Combinations.
Dr. Genserico G. Jayme, Annapolis, Brazil, Cephalic Tetanus of Ocular Origin.
Dr. Pereira Gomes, São Paulo, Brazil, Tumors of the Optic Nerve.
Dr. Tomas R. Yanes, Habana, Cuba, Dacryocystorhinostomy.
Dr. Carlos Charlin, Santiago, Chile, Occult Tuberculosis of the Eye.
Dr. William L. Benedict, Rochester, Minn., Orbital Hyperostosis.
Dr. Daniel B. Kirby, New York, Congenital Bilateral Colobomata of the Upper and Lower Eyelids: Plastic Surgical Correction.
Drs. Alan C. Woods and Jack S. Guyton, Baltimore, Chemotherapy in Ophthalmology.
Dr. Samuel Hanford McKee, Montreal, Canada, Observations on the Fundus Oculi in Diabetes Mellitus.

It is expected that the Pan American congress will be placed on a permanent basis during this meeting. The committee that has arranged the first congress is made up of Drs. Harry S. Gradle, Chicago; Conrad Berens, New York, and Moacyr E. Alvaro, São Paulo, Brazil.

CANADA

Personal.—Dr. Charles W. MacMillan, St. John, has been appointed chief medical officer for the province of New Brunswick.——Dr. George F. Stephens, superintendent of the Winnipeg General Hospital, Winnipeg, Man., for twenty-one years, has been appointed superintendent of the Royal Victoria Hospital, Montreal.

FOREIGN

Hospital Equipment for China.—A fund contributed by the Committee for Medical Aid to China in Victoria, B. C., Canada, has been used to establish a library in connection with the medical school at Yenan and to purchase an x-ray machine for the Kuomaio Model Hospital in memory of Dr. Norman Bethune, Canadian surgeon who went to China in 1937. Dr. Bethune died Nov. 13, 1939, of septicemia following an injury received while operating. In addition to working with the wounded immediately behind the lines, Dr. Bethune organized the International Peace Hospitals, which now include four base hospitals, a transport network for supplies and mobile medical teams. The library will be an invaluable aid to medical students who have been studying with roughly duplicated notes and an almost total lack of reference material, according to the China Defense League *Newsletter*. The hospitals are in urgent need of surgical instruments and equipment, including many types of forceps, scissors, Luer syringes, hypodermic needles and various kinds of rubber tubes.

CORRECTION

Health Department Headquarters Remain in Sacramento.—The director of the state department of public health of California, Dr. Bertram P. Brown, writes that headquarters of the department will remain in Sacramento with branch offices in Los Angeles and San Francisco as heretofore. An announcement that the headquarters of the department had been moved to Los Angeles, published in THE JOURNAL, September 7, page 867, was based on reports appearing in the newspapers.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Aug. 17, 1940.

Hysterical Contractures Following War Injuries

At the Royal Society of Medicine Sir Arthur Hurst opened a discussion on hysterical contractures following war injuries. In civil life contractures following injuries were comparatively rare but after war injuries were frequent. During the last war the nature of these contractures was much discussed but only toward the end did it become almost universally recognized that they were hysterical and could be quickly cured by proper treatment. The most common contracture followed injury to the soft parts of any type. Sometimes there was no wound, only a twist or a sprain. A limb was sometimes found completely stiff after amputation of a hammer toe or removal of a semilunar cartilage, but this was amenable to psychotherapy. The postures were of great variety. The commonest developed in the hand and were of two main kinds: with the fingers stiffened in extension or tightly flexed into the palm. One patient's hand was contracted for two and one-half years and, when cured at a single sitting and the hand was opened, the nails had grown deeply into the palm. Fixation of the wrist was infrequent; of the elbow, frequent; of the shoulder held tightly to the side, occasional. In a number of cases the toes were affected and the patient walked on the ball of the foot. The knee and the hip were often fixed. Immediately after the injury the patient adopted the most comfortable position and this might develop into a contraction. In some cases the limb was put into a splint and after its removal maintained the same position. The limb was fixed because the patient had lost the idea of movement. This could be prevented by putting the limb through complete movements when dressings were removed. Contractures were most likely when the patient was sent to the physical therapy department. Babinski made the mistake of concluding that contractures were reflex and therefore organic in origin and not hysterical. What led him to this was the remarkable trophic changes in patients with deficient circulation following disuse of a part. The skin became wrinkled, blue, thin and shiny and the finger nails gray and lusterless, grooved and brittle; the bones showed abnormal translucency. But all these changes, simulating the trophic changes following nerve injury, were simply the result of disuse and deficient circulation.

Treatment in the early days of the war consisted in a certain amount of suggestion and occasional hypnotism, but later Hurst and his colleagues found simpler methods of psychotherapy more valuable. The patients were not commonly hysterical and never had had "shell shock." Persuasion, manipulation and reeducation were found effective and the ideal patient was cured merely by telling him what to do. It was explained to him how the contracture developed, that it was necessary to rest the limb after the injury, but that when the splint and bandage were taken away the limb should be moved. The patient was taught to relax the limb, and the physician moved the affected part a little and allowed it to relax again.

In the discussion Dr. J. B. Mennell (physical therapist) said that if there was one condition more than another with which the physical therapist should not interfere it was these contractures. Unraveling them by force was a barbarous method and the contractures recurred. Colonel Henry Yellowlees (psychiatrist) did not find Hurst's one remark about the psychopathology—that the patient lost the idea of movement—satisfying. Hurst replied that the important thing was to get results. He believed that, if he ranged the ten medical officers who worked under him in order of their success, the one who would be last

or nearly last was the skilled psychotherapist. The worst cases of shell shock seen after the war of 1914-1918 were those which had been under the care of psychologists in France, who had carried out experiments in hypnotism with disastrous results. The president (Mr. Zachary Cope) remarked that Sir Arthur Hurst had stated that in some cases the joints could not be moved even under general anesthesia. Surely under deep anesthesia a joint not absolutely ankylosed would be movable. Hurst replied that he had seen a soldier whose knees were rigidly extended. He had had many spa treatments without improvement. Under a general anesthetic he did not relax, but under psychotherapy relaxation was gradually obtained. It was extremely difficult to explain such cases.

The Improvement of Bread

The Medical Research Council has issued a statement on the advantages of bread made from flour of higher extraction than that now in use. Flour should contain the germ of the wheat, as much as possible of the aleuron layer, and the finer portions of bran. Instead of consisting of about 70 per cent of the wheat grain, as at present, flour should contain from 80 to 85 per cent. The content of certain vitamins, all minerals and fat would thus be improved. This improvement would benefit most persons of small income whose power to purchase protective foods is limited. The minimum daily requirement of vitamin B_1 is from 300 to 500 international units. The pound loaf made from white flour of 70 per cent extraction gives from 80 to 160 units; from flour of 80 to 85 per cent extraction from 300 to 450 units, almost the total requirement. The Accessory Food Factors Committee of the Lister Institute and the Medical Research Council examined the ways in which the health of the people might be benefited by improving the value of wheaten bread and concluded that this change in one dietary essential alone would benefit greatly the health of children and adults of all classes. There would also be benefit from increase of other members of the B complex, such as riboflavin, and of vitamin E. The carotene (provitamin A) content would also be improved, if not previously destroyed by bleaching. The committee therefore condemns the bleaching of flour by oxidizing agents, such as nitrogen chloride and nitrogen peroxide. Increased fat content would be another benefit.

The total mineral content would be doubled. The daily requirement of iron may be taken as 10 mg. The pound loaf of 70 per cent extraction supplies only 5 mg. Anemia from iron deficiency is common among poorer women, especially in pregnancy, and among their infants. The daily requirement of calcium may be taken as 500 mg. The pound loaf of 70 per cent extraction contains less than 150 mg. Insufficiency of calcium is an important defect in the British diet but would not be compensated by increased extraction of flour. Bread is a poor source of calcium. The foods most rich in calcium are milk, cheese and green vegetables.

There are possible disadvantages from the increased extraction of flour. Flours of high extraction, if coarsely ground, are slightly less utilized than finer flour. For this reason 80 to 85 per cent extraction is recommended; it represents a fraction of the wheat grain in which improvement in the nutritive value of the flour is pronounced but in which decreased utilization has scarcely begun. But if a flour of 90 or even 100 per cent extraction could be obtained in finely ground condition, the nutritive advantages would be increased and the disadvantages of incomplete utilization would tend to disappear. Phytic acid precipitates calcium, so that it cannot be absorbed. Although high extraction flour contributes more calcium to the diet, it also contributes more phytic acid. Because of the need of more calcium in the British diet and its deficiency in bread, whatever the degree of extraction of the flour, the committee recommends the addition of calcium salts to bread, while at the same time the foods rich in calcium should be promoted. The committee condemns the use of alkaline baking powder because it destroys the vitamin B_1 content of bread.

Provision for the Treatment of Air Raid Casualties

Speaking at a luncheon of the National Defense Public Interest Committee Mr. Malcolm MacDonald, minister of health, stated that there were now 1,800 fixed first aid posts in England and Wales, 800 mobile first aid posts, 14,000 ambulances and 15,000 ordinary cars waiting to carry sitting patients. The staff of the first aid section numbered about 100,000 persons. The Ministry of Health was also responsible for the treatment of all cases resulting from enemy action and for the hospital treatment of all but a small number of military casualties on any battle front in this country or outside. The organization passed its preliminary test at the time of the evacuation of Dunkirk, and the medical staff was astonished at the rapidity with which the patients recovered. That confirmed the high physical quality of our men and was also partly due, no doubt, to the excellent modern nursing and doctoring.

PLASMA TRANSFUSION ADOPTED

The recent suggestion to substitute for transfusion of whole blood plasma transfusion, because it is equally effective in cases of shock and is attended with less risk of reactions, has been adopted with good results. Mr. MacDonald stated that the plasma would keep indefinitely and so the call on blood donors had been reduced. But a further advance had been made. Plasma stored in bottles was not easily transportable. So by evaporation it was reduced to a white powder, by the addition of water to which the original liquid with all its properties could be reconstituted.

Marriages

RAYMOND LOUIS EVANS, Cincinnati, to Miss Augusta Dorrance Farnham of Wilkes-Barre, Pa., at Montrose, Pa., August 31.

DALE EMERSON BARBER, Oakland, Calif., to Miss Barbara Way of Washington, D. C., in San Francisco, August 24.

VICTOR R. KRUEGER, Bonduel, Wis., to Miss Blanche Lamberton of Melrose, Minn., in Duluth, Minn., June 25.

THOMAS E. CANNING, Colville, Wash., to Miss Mary Lou Ralph of Spokane at Clark Ford, Idaho, August 3.

HENRY ANDREWS COTTON JR., Trenton, N. J., to Miss Anne Tooker at South Williamstown, Mass., August 31.

THEODORE SCHLOSSBACH, Ocean Grove, N. J., to Miss Eleanor Pegley Krause at Asbury Park, August 17.

SAMUEL BANCROFT FLUKE, Harrisburg, Pa., to Miss Florence Hardy of Washington, D. C., June 15.

VLADIMIR C. FLOWERS, Ithaca, N. Y., to Miss Alice Victoria Rex of Oak Park, Ill., August 31.

CLAUDE K. LINDLER to Miss Margaret Maxwell Ward, both of Columbia, S. C., August 24.

GEORGE M. KLITCH, Harrisburg, Pa., to Miss Ruthanna Mark of Hagerstown, Md., June 22.

JESSE J. HEATON, Tiffin, Ohio, to Miss Inez A. Johnson of McCutchenville, August 1.

JOSEPH DUDGEON WALKER to Mrs. Nannie Dunlap, both of Houston, Texas, July 25.

MARGARET PAXSON, Pottsville, Pa., to Mr. Harry F. Brian of Lancaster, August 17.

RAYMOND C. HACKER to Miss Florence A. Mease, both of Philadelphia, June 29.

LUDWIG J. O'BLAZNEY, Simpson, Pa., to Miss Wanda Fasceski, August 31.

JAMES L. KING to Miss Helen Morrow, both of Florence, S. C., in August.

DONALD E. MORRISON, Penbrook, Pa., to Miss Alice Louise Gillan, June 12.

Deaths

Maude Elizabeth Seymour Abbott, Montreal, Que., Canada; University of Bishop College Faculty of Medicine, Montreal, 1894; honorary M.D., C.M., McGill University, 1910; formerly assistant professor of medical research and curator of the medical museum, McGill University Faculty of Medicine and lecturer of pathology from 1912 to 1923; was acting curator of the Canadian Army Medical Museum; professor of pathology and bacteriology at the Woman's Medical College of Pennsylvania, Philadelphia, from 1923 to 1925; member of the American Association of Anatomists and the American Association of Pathologists and Bacteriologists; permanent secretary-treasurer and one of the founders of the International Association of Medical Museums; editor of the *Journal of Technical Methods* and *Bulletin of the International Association of Medical Museums* from 1907 to 1938; managing editor of the "Osler Memorial Volume"; on the editorial board of the *Canadian Medical Association Journal;* author of "Classified Bibliography of Sir William Osler's Publications," "Atlas of Congenital Cardiac Disease" and "Historical Sketch of the Medical Faculty of McGill"; was awarded the degree of doctor of laws honoris causa from McGill University; aged 71; died, September 2, of cerebral hemorrhage.

Harold M. Hays ✠ New York; Columbia University College of Physicians and Surgeons, New York, 1905; instructor of otolaryngology at his alma mater from 1914 to 1922; associate professor of laryngology at the New York Polyclinic from 1914 to 1917; member of the American Academy of Ophthalmology and Otolaryngology and the American Laryngological, Rhinological and Otological Society; fellow of the American College of Surgeons; past president of the American Federation of Organizations for the Hard of Hearing; founder, president and director of the New York League for the Hard of Hearing; served during the World War; director of the Hebrew Association for the Deaf; was president of the Association of Private Hospitals of Greater New York; medical director of the Park East Hospital and the Park West Hospital; consulting otologist to the Convalescent Home of Hebrew Children, Rockaway Park, and St. Joseph Hospital, Far Rockaway; consulting laryngologist to the Sing Sing Prison Hospital, Ossining; author of "Diseases of Nose, Throat and Ear" and "Modern Conception of Deafness"; aged 59; died, August 20, of coronary thrombosis.

Charles Francis Nassau ✠ Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1891; Jefferson Medical College of Philadelphia, 1906; clinical professor of surgery at the Jefferson Medical College; past president of the Philadelphia County Medical Society; honorary president of the John Chalmers Da Costa Foundation; fellow of the American College of Surgeons; formerly director of public health of Philadelphia; served during the World War; chief surgeon, Frankford Hospital; surgeon, St. Joseph's Hospital and Girard College; assistant surgeon, Jefferson Hospital; consulting surgeon, Mount Sinai Hospital, Kensington Hospital for Women and Rush Hospital for Consumption and Allied Diseases, Philadelphia, and the Pottstown (Pa.) Hospital; aged 71; died, August 11, in the Easton (Pa.) Hospital of coronary occlusion.

John Crean Cardwell, Brooklyn; University of the City of New York Medical Department, 1888; member of the Medical Society of the State of New York; instructor in physiology at Harvard Medical School, Boston, from 1891 to 1893; instructor in physiology at the Long Island College Hospital from 1900 to 1904, lecturer from 1904 to 1908, assistant professor from 1908 to 1910, adjunct professor 1910-1911, associate professor from 1911 to 1913, professor of physiology and acting professor of pharmacology from 1919 to 1928, professor of physiology and pharmacology from 1928 to 1930 and since 1932 emeritus professor; member of the American Association of Anatomists; aged 74; died, August 3.

Larkin Smith ✠ Nashville, Tenn.; University of Nashville Medical Department, 1888; Vanderbilt University School of Medicine, Nashville, 1889; demonstrator of histology, pathology and microscopy from 1889 to 1898, professor of hygiene and preventive medicine, associate professor of pathology from 1909 to 1915, instructor in medicine from 1915 to 1925 and instructor in clinical medicine from 1925 to 1928 at the Vanderbilt University School of Medicine; at one time secretary of the Tennessee State Medical Association; formerly health officer of Nashville; served during the World War; formerly on the staff of the Vanderbilt Hospital; aged 74; died, July 17, of pernicious anemia and diabetes mellitus.

James McKenty, Winnipeg, Man., Canada; Queen's University Faculty of Medicine, Kingston, Ont., 1890; served at various times as lecturer in anatomy, assistant professor in clinical medicine, associate professor of surgery and emeritus professor of surgery at the University of Manitoba Faculty of Medicine; was president of the Winnipeg Medical Society; fellow of the American College of Surgeons; for many years on the staffs of St. Boniface, Misericordia and St. Joseph's hospitals; aged 74; died, August 11, of cerebral hemorrhage.

Robert Kingman, Brooklyn; Long Island College Hospital, Brooklyn, 1899; formerly clinical instructor in neurology at his alma mater; past secretary and vice president of the Brooklyn Neurological Society; served as New York State Examiner in Lunacy, and New York State Examiner of Mental Defectives; was consulting neuropsychiatrist in the United States Public Health Service hospitals; on the staff of the Kings County Hospital and the Greenpoint Hospital; aged 64; died, August 7, of coronary thrombosis.

John Archer Hatchett, Oklahoma City; Missouri Medical College, St. Louis, 1884; member of the House of Delegates of the American Medical Association, 1905-1906, and Second Vice President in 1908; member of the Oklahoma State Medical Association; past president of the Oklahoma County Medical Society; professor emeritus of obstetrics at the University of Oklahoma School of Medicine; at one time on the staff of the University Hospital; aged 87; died, August 16, of arteriosclerosis and pneumonia.

Howard Leighton Updegraff ✠ Los Angeles; University of Nebraska College of Medicine, Omaha, 1919; fellow of the American College of Surgeons; honorary member of the Royal Australasian Medical Society; member of the Society of Plastic and Reconstructive Surgery; on the staffs of the Hollywood Presbyterian, Cedars of Lebanon, Orthopedic and Methodist hospitals; associate editor of the *American Journal of Surgery*; aged 43; died, August 8, of acute hemorrhagic pancreatitis.

Augustus Thorndike, Boston; Harvard Medical School, Boston, 1888; member of the Massachusetts Medical Society; past president of the American Orthopedic Association; formerly instructor of orthopedics at his alma mater; at one time assistant visiting surgeon to the House of the Good Samaritan and assistant surgeon to the Children's Hospital; author of "A Manual of Orthopedic Surgery," published in 1907; aged 77; died, August 23, in Bar Harbor, Maine, of heart disease.

Joseph Brock Harrison ✠ Westfield, N. J.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1876; for many years member of the board of education and president of the board of health; past president of the Union County Medical Society; on the courtesy staff of the Muhlenberg Hospital, Plainfield, and the Elizabeth (N. J.) General Hospital; aged 88; died, August 25, of uremia, hypertrophy of the prostate and myocarditis.

Anson James Singer, East Stroudsburg, Pa.; University of the City of New York Medical Department, 1883; member of the Medical Society of the State of Pennsylvania; past president of the Monroe County Medical Society; was president of the board of trustees of the State Teachers College; one time mayor; formerly on the staff of the General Hospital of Monroe County; aged 82; died, July 29.

Walter Alonzo Bartlett, Manchester, N. H.; Dartmouth Medical School, Hanover, 1911; member of the New Hampshire Medical Society; formerly member of the board of education; on the staff of the Hillsborough County General Hospital, Grasmere, and the Sacred Heart Hospital; aged 50; died, August 12, in the New Hampshire State Sanatorium, Glencliff, of pulmonary tuberculosis.

William Henry Howell ✠ Altoona, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1899; fellow of the American College of Surgeons; past president of the Blair County Medical Society; on the staff of the Altoona Hospital and Mercy Hospital; aged 67; died, August 13, in the Annie M. Warner Hospital, Gettysburg, of cerebral hemorrhage.

Arthur Lloyd Chambers ✠ New York; New York Homeopathic Medical College and Flower Hospital, New York, 1914; associate professor of ophthalmology at his alma mater; fellow of the American College of Surgeons; on the staffs of the New York Ophthalmic Hospital, Flower and Fifth Avenue hospitals and the Metropolitan Hospital; aged 51; died, August 14.

Thomas Albert Sinclair, Houston, Texas; Keokuk Medical College, College of Physicians and Surgeons, Keokuk, Iowa, 1905; member of the State Medical Association of Texas; medical superintendent of the Heights Clinic-Hospital; aged 67;

member of the city health department from 1920 to 1928; died, July 26, of heart disease.

Henry LeBaron Peters ✠ Bridgeport, Conn.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1907; for many years medical examiner of Bridgeport; attending physician and director of the pathologic and bacteriologic laboratory of the Bridgeport Hospital; aged 58; died in August of coronary thrombosis.

William Joseph Leonard, Provincetown, Mass.; College of Physicians and Surgeons, Baltimore, 1896; served during the World War; formerly police department surgeon and city physician of Springfield; at one time on the staffs of the Mercy Hospital and the City of Springfield Infirmary, Springfield; aged 70; died, July 25.

Bleeker James Knapp ✠ Evansville, Ind.; Rush Medical College, Chicago, 1901; member of the American Academy of Ophthalmology and Oto-Laryngology; fellow of the American College of Surgeons; aged 63; surgeon to the Protestant Deaconess Hospital, where he died, August 20, of chronic nephritis and uremia.

Ralph Harpel Dunlap, Bellevue, Pa.; Johns Hopkins University School of Medicine, Baltimore, 1919; member of the Medical Society of the State of Pennsylvania; on the staff of St. John's General Hospital, Pittsburgh, and the Salvation Army Woman's Home and Hospital; aged 48; died, August 8.

Maximilian Joseph Kern, St. Cloud, Minn.; John A. Creighton Medical College, Omaha, 1904; member of the Minnesota State Medical Association; for many years county coroner, and member of the city council; aged 59; died, August 10, of hypertension and cerebral hemorrhage.

Elisha C. Chew ✠ Atlantic City, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1891; past president of the Atlantic County Medical Society; formerly police surgeon; on the staff of the Atlantic City Hospital; aged 73; died, August 5, of chronic fibroid phthisis.

Joseph Montgomery Casey, Fort Madison, Iowa; Rush Medical College, Chicago, 1888; member of the Iowa State Medical Society; aged 75; on the staff of the Sacred Heart Hospital and the Atchison, Topeka and Santa Fe Railway Hospital, where he died, July 30, of myocarditis.

Warren Bunting Shaner, Pottstown, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1882; member of the Medical Society of the State of Pennsylvania; for many years on the staff and secretary of the staff of the Pottstown Hospital; aged 80; died, July 15.

Edward H. White ✠ Cumberland, Md.; Baltimore Medical College, 1899; past president of the Allegany and Garrett Counties Medical Society; at one time city and county health officer; on the staffs of the Allegany and Memorial hospitals; aged 70; died, July 13.

Robert Edward Lee Thacker ✠ Lexington, Okla.; University of Louisville (Ky.) Medical Department, 1893; served during the World War; aged 74; died, July 10, in the Wesley Hospital, Oklahoma City, of hypertensive heart disease and prostatic hypertrophy.

William Wilberforce Farr, Philadelphia; University of Pennsylvania Department of Medicine, Philadelphia, 1887; served during the World War; aged 75; died, August 19, in the Germantown Dispensary and Hospital of bronchopneumonia and diabetes mellitus.

Napoleon Gustavus Gewinner, Macon, Ga.; Medical College of the State of South Carolina, Charleston, 1879; member of the Medical Association of Georgia; aged 82; died, August 19, in Atlanta of acute intestinal obstruction and mesenteric thrombosis.

Henry Grady Lassiter ✠ Weldon, N. C.; Jefferson Medical College of Philadelphia, 1918; past president of the Halifax County Medical Society; aged 48; died, August 1, in the Roanoke Rapids (N. C.) Hospital of cerebral hemorrhage and hypertension.

William Hugh Hamley, Lake Providence, La.; University of Tennessee College of Medicine, Memphis, 1914; member of the Louisiana State Medical Society; served during the World War; aged 51; died, August 6, in Vicksburg, Miss., of cirrhosis of the liver.

William Albert Jolley, North Little Rock, Ark.; Jefferson Medical College of Philadelphia, 1896; member of the American Psychiatric Association; served during the World War; on the staff of the Veterans Administration Facility; aged 68; died, August 2.

Arthur Clinton Hendrick, Toronto, Ont., Canada; University of Toronto Faculty of Medicine, 1900; fellow of the American College of Surgeons; on the staff of the Toronto General Hospital and the Grace Hospital; aged 66; died, August 1.

Willet W. Binion, Benevolence, Ga.; Atlanta Medical College, 1885; member of the Medical Association of Georgia; for many years member of the county board of education; aged 80; died, August 13, of chronic nephritis and arteriosclerosis.

William Henry Lehner, Brentwood, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1895; member of the Medical Society of the State of Pennsylvania; formerly on the staff of the Southside Hospital, Pittsburgh; aged 76; died, July 21.

Ellen Elizabeth Brown, Graterford, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1881; member of the Medical Society of the State of Pennsylvania; for many years on the staff of the Chester (Pa.) Hospital; aged 91; died, July 29.

Lawrence Alvies Mendonsa, St. Louis; St. Louis College of Physicians and Surgeons, 1906; member of the Missouri State Medical Association; secretary of St. Louis County Medical Society; aged 58; died, July 17, in the Central Hospital.

Jacob S. Thompson, Stephens, Ark.; University of Louisville (Ky.) Medical Department, 1882; past president of the Ouachita County Medical Society; at various times president of the school board and bank president; aged 83; died, July 10.

Friedrich Schiff, New York; Friedrich-Wilhelms-Universität Medizinische Fakultät, Berlin, Prussia, 1913; member of the Medical Society of the State of New York; bacteriologist on the staff of the Beth Israel Hospital; aged 51; died, July 30.

Job Thigpen Cater, Montgomery, Ala.; Rush Medical College, Chicago, 1930; member of the Medical Association of the State of Alabama and the Association for Research in Ophthalmology; aged 39; died, July 3, in the Hubbard Hospital.

Harry Douglas Thompson ✠ Beverly Hills, Calif.; College of Physicians and Surgeons, Los Angeles, 1918; on the staff of the Presbyterian Hospital-Olmsted Memorial, and chairman of the library committee; aged 48; died, July 3.

John Calvin Simon, Cleveland; Eclectic Medical Institute, Cincinnati, 1889; formerly county coroner; on the staff of the Grace Hospital and St. John's Hospital; aged 73; died, August 6, in Olmsted Falls, Ohio, of coronary occlusion.

Nicholas R. Engels, Chicago; Rush Medical College, Chicago, 1896; member of the Illinois State Medical Society; on the staff of St. Bernard's Hospital; aged 76; died, August 11, of cerebral hemorrhage and arteriosclerosis.

Alphonse Lagaci, Franklin, N. H.; M.B., School of Medicine and Surgery of Montreal, Faculty of Medicine of the University of Laval at Montreal, 1907, and M.D. in 1909; for many years mayor; aged 58; died, July 26.

James Garrity ✠ Chicago; Rush Medical College, Chicago, 1904; aged 60; for many years on the staff of the West Suburban Hospital, Oak Park, Ill., where he died, August 31, of injuries received in an automobile accident.

Lawrence Robert Harris, Galveston, Texas; University of Texas School of Medicine, Galveston, 1907; member of the State Medical Association of Texas; aged 57; died, August 6, of pulmonary edema and chronic nephritis.

James Anderson Gessing, Oak Park, Ill.; National Medical College, Chicago, 1897; member of the Illinois State Medical Society; aged 71; died, August 22, in the West Suburban Hospital of chronic myocarditis.

William Tone McMannis, New York; College of Physicians and Surgeons, medical department of Columbia College, New York, 1885; member of the Medical Society of the State of New York; aged 76; died, July 14.

Charles Leonard Randall, Salamanca, N. Y.; University of Buffalo School of Medicine, 1895; formerly county coroner and school physician; served during the World War; aged 73; died, July 27, of coronary thrombosis.

John Louis Hoffman ✠ Ashland, Pa.; University of Pennsylvania Medical Department, 1886; served during the World War; aged 76; died, August 11, in the Ashland State Hospital of myocarditis and arteriosclerosis.

Bernard DeKoven, Chicago; Columbia University College of Physicians and Surgeons, New York, 1904; aged 63; died, August 11, in the Michael Reese Hospital of myocarditis and chronic myelogenous leukemia.

Julius Wesley Hill, Richmond, Ky.; University of Louisville Medical Department, 1905; member of the Kentucky State Medical Association; aged 60; died, August 17, of arteriosclerosis and chronic nephritis.

Fanny Elizah Shutts, Los Angeles; Hahnemann Medical College of the Pacific, San Francisco, 1916; for many years member of the city health department; aged 65; died, July 5, in the Roosevelt Sanitarium.

Robert Ziegmond Garber, Ann Arbor, Mich.; University of Michigan Medical School, Ann Arbor, 1938; aged 26; died, August 6, in the University Hospital of pulmonary and intestinal tuberculosis.

Uriel Pierce Haw, Benton, Mo.; Vanderbilt University School of Medicine, Nashville, Tenn., 1898; member of the Missouri State Medical Association; aged 67; was shot and killed, July 23.

Isaac Newton Adams, Pineville, La.; Memphis (Tenn.) Hospital Medical College, 1901; member of the Louisiana State Medical Society; served during the World War; aged 63; died, July 25.

John Palmer Hollenback, New York; Creighton University School of Medicine, Omaha, 1937; resident surgeon on the staff of the Lenox Hill Hospital; aged 28; was found dead, July 21.

Bernard Reamy Le Roy, Stoutsville, Ohio; Western Reserve University Medical Department, Cleveland, 1885; veteran of the Spanish-American War; aged 80; died in July.

John A. Brady, Louisville, Ky.; University of Louisville (Ky.) Medical Department, 1893; served during the World War; aged 69; died, July 11, in the Kentucky Baptist Hospital.

Max Rosebery, New York; College of Physicians and Surgeons, medical department of Columbia College, New York, 1892; served during the World War; aged 71; died in July.

George Gordon Griffith, Spurgeon, Ind; University of Louisville (Ky.) Medical Department, 1913; member of the Indiana State Medical Association; aged 50; died, July 3.

John Albert Reese, Detour, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1906; member of the Michigan State Medical Society; aged 60; died, July 15.

Joseph Clyde McCartney, Pelotas, Brazil; Medico-Chirurgical College of Philadelphia, 1886; also a dentist; aged 80; died, June 24, at sea while aboard the S. S. *Brazil*.

James Bray Bradley, Eaton Rapids, Mich.; Rush Medical College, Chicago, 1886; member of the Michigan State Medical Society; at one time mayor; aged 81; died, July 4.

William Wesley Hall, McLeansboro, Ill.; Rush Medical College, Chicago, 1883; member of the Illinois State Medical Society; aged 78; died, August 17, of carcinoma.

Thomas Richard Butler, Lexington, Mo.; Bellevue Hospital Medical College, New York, 1885; member of the Missouri State Medical Association; aged 77; died, July 4.

Llewelyn David Roberts, Hamilton, Mont.; Tulane University of Louisiana School of Medicine, New Orleans, 1938; aged 30; died, July 12, of chronic endocarditis.

Ernest Eugene Thompson, Red Bluff, Calif.; Cooper Medical College, San Francisco, 1900; member of the California Medical Association; aged 64; died, July 18.

John Camden Cochran, St. Marys, Pa.; Dartmouth Medical School, Hanover, N. H., 1890; Jefferson Medical College of Philadelphia, 1890; aged 84; died, July 18.

William E. Ford, Arlington, Va.; Maryland Medical College, Baltimore, 1909; served during the World War; aged 59; died, August 14, of diabetes mellitus.

Elmer C. Bond, Hanford, Calif.; California Medical College, San Francisco, 1899; member of the California Medical Association; aged 66; died, July 8.

Joseph David Michie ✠ Childress, Texas; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1898; aged 67; died in July.

John Joseph Whoriskey ✠ Boston; Harvard Medical School, Boston, 1899; on the staff of St. Elizabeth's Hospital; aged 64; died, July 26, in Scituate.

Henry B. Gifford, Juda, Wis.; Rush Medical College, Chicago, 1883; aged 82; died, July 15, in Monroe of cerebral hemorrhage and chronic arthritis.

Ward Watson Wiers, Royal Oak, Mich.; Detroit College of Medicine, 1911; member of the Michigan State Medical Society; aged 64; died, July 13.

Louis William Rehbein, Los Angeles; Jefferson Medical College of Philadelphia, 1901; aged 68; died, July 13, of cerebral hemorrhage and arteriosclerosis.

Purvis Alexander Spain, Brooklyn; University and Bellevue Hospital Medical College, New York, 1899; aged 67; died, July 13, in the Wade Hospital.

B. Frank Eckman, Coral Gables, Fla.; Medical College of Ohio, Cincinnati, 1890; member of the Florida Medical Association; aged 72; died, July 9.

Israel Goldstein, Brooklyn; Columbia University College of Physicians and Surgeons, New York, 1922; aged 43; died, August 3, of angina pectoris.

George Walter Harding, Warsaw, Ind.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1886; aged 81; died, July 25.

Elbert Earl Freeman, Greentown, Ind.; Hering Medical College, Chicago, 1908; aged 59; died, August 11, of purpura haemorrhagica.

Edward Laughton Quirk, Aylmer (East), Que., Canada; McGill University Faculty of Medicine, Montreal, 1888; died about June 15.

William Patterson, Montreal, Que., Canada; University of Bishop College Faculty of Medicine, Montreal, 1884; aged 92; died, June 29.

William Frank Alvey, Louisville, Ky.; Chattanooga (Tenn.) Medical College, 1898; served during the World War; aged 67; died, July 29.

Oran Newton, Taft, Calif.; California Eclectic Medical College, Los Angeles, 1910; formerly health officer; aged 57; died, July 22.

Charles Augustus Ruflin ✠ Louisville, Ohio; University of Wooster Medical Department, Cleveland, 1906; aged 60; died, July 30.

William Franklin Markley, Follett, Texas; University of Kansas School of Medicine, Kansas City, Kan., 1906; aged 66; died, July 9.

Hilborn Wilton Harris ✠ Canton, Mo.; Missouri Medical College, St. Louis, 1888; aged 76; died, August 12, of coronary thrombosis.

George E. Kerns, Galion, Ohio; Eclectic Medical Institute, Cincinnati, 1903; aged 67; died, August 13, in Cleveland of pneumonia.

Arthur Philip Damerow ✠ Englewood, Colo.; University of Colorado School of Medicine, Denver, 1927; aged 40; died, June 5.

Joseph Aloysius Duffey ✠ Cincinnati; Eclectic Medical College, 1913; served during the World War; aged 49; died, July 9.

William F. Kellogg, Ethridge, Tenn.; University of the South Medical Department, Sewanee, 1898; aged 81; died, July 3.

Percy Leroy Jones, Lenexa, Kan.; Eclectic Medical Institute, Cincinnati, 1905; aged 62; died, June 26, of pneumonia.

James Addison Bell, Decatur, Ga.; Louisville (Ky.) Medical College, 1905; aged 59; died, July 7, of coronary disease.

Albert Jerome Britt, Philadelphia; Jefferson Medical College of Philadelphia, 1893; aged 68; died, July 26, in Rydal.

Mark Neumann, San Francisco; University of the City of New York Medical Department, 1880; aged 83; died, May 17.

Wilfred Joseph Heringer, Port Arthur, Ont., Canada; Manitoba Medical College, Winnipeg, 1913; died, June 30.

Robert a'Beckett Stephenson, Inglewood, Calif.; Rush Medical College, Chicago, 1903; aged 65; died, May 17.

James A. Delaney, Bristol, Tenn.; Hospital College of Medicine, Louisville, Ky., 1895; aged 70; died, July 23.

George Lyman Woods, Knoxville, Tenn.; Medical School of Maine, Portland, 1879; aged 90; died, July 28.

Alonzo Bittle Curtis, Lower Peach Tree, Ala.; Medical College of Alabama, Mobile, 1882; died, July 23.

Oliver I. Hess, Scottdale, Pa.; Kentucky School of Medicine, Louisville, 1894; aged 86; died, July 9.

J. M. Parks, Elkhart, Texas (licensed in Texas, under the act of 1907); aged 84; died, July 16.

John C. Luke, Ocilla, Ga.; Louisville (Ky.) Medical College, 1893; aged 70; died, July 1.

R. Pierce White, Stovall, Ga.; Atlanta Medical College, 1884; aged 80; died, July 18.

Bureau of Investigation

DARK AGES STILL WITH US

Seven U. S. Post Office Fraud Orders Against "Cure-Alls"

There can be no such remedy as a "cure-all." By this time every one ought to know that not even sulfanilamide is a panacea. Nevertheless, some concerns still find it profitable to advocate a remedy or a line of remedies for the treatment of practically everything. There is evidence to indicate that one promoter who at various times seems to have interested himself in some of the above-named products, was apparently not satisfied with the extent of this fraud and included in his advertising some of the old Albert Abrams hokum: "A Complete Blood Test—Radio-Electronic Diagnosis and Treatments." "One Drop of Your Blood" said he, would reveal whether you had "cancer, tuberculosis, blood infections or other ailments" and whether these conditions would be "curable or incurable" in your case.

Much more in the way of history of some of the concerns named in the tables could be developed in this article from the files of the Bureau of Investigation. At this late date however it is hoped that, since these remedies have their appeal only to the unintelligent, these promotions are not of sufficient importance to warrant separate articles in the pages of a scientific publication.

The group of seven were subjects of fraud orders issued during the past year and serve to illustrate the extent to which such promoters carry on their activities and also to illustrate the laudable action of the Post Office Department in these cases. Table 1 gives the name and location of each firm and the names of the remedies which were promoted, while table 2 indicates the conditions in which these remedies were advocated. Of special note are those which were apparently promoted for any ailment or disorder as well as those which were suggested as remedies for diabetes, diphtheria, tuberculosis, sleeping sickness, insanity and syphilis.

The Post Office Department is to be commended for refusing the use of the United States mails to these concerns. It is to be hoped that all other such remedies will be subjects of similar fraud orders issued at an early date. It is also to be hoped that whatever portion of the American public comprises the purchasers of these remedies will soon be educated to the point where the sale of such items reaches absolute zero.

TABLE 1.—*Fraud Orders Referred to in This Article*

Names of Individuals and Companies	Location	Remedies Named	Date of Issue	Order Number
Arrowhead Indian Herbs Company... Dewey Conway, Jodie Conway	Chico, Calif.	Remedy No. 19-D; No. 28-D; No. 138-D; No. 240-D; No. 297-D; No. 6-D; No. 7-D; No. 14-D; No. 104-D; No. 39-L	July 30, 1940	14417
Botanical Medicine Company..... Dr. W. B. Goebel	Kannapolis, N. C.	Gall Bladder Special; Pyorrhea Treatment; Trifolium; Lav-I-Ton; Ironite; Black Spirit; Femidyne; Ey-No-La; Hem-I-Rin; Kre-Cal	Jan. 22, 1940	13700
Crocker's Asthma & Lung Trouble Medicine Company James Crocker	Indianapolis	Drinking Water No. 29; Syrup No. 377; Tea No. 370	Jan. 29, 1940	13723
H. W. Lange & Son..... Lange & Son F. W. Lange	Portland, Ore.	Lang's Mineral Wonder; Lang's Mineral Ointment; Lang's Female Suppositories	May 8, 1940	14112
Morehead & Co. ..... E. H. Morehead & Co.	Denver	Rocky Mountain Mineral Wonder; Mineral Wonder Laxative	Feb. 12, 1940	13773
Prof. C. A. Isbell.....	Colfax, Calif.	Isbell's Mineral	July 15, 1940	14349
Theodore M. Moore..... Prof. Theodore M. Moore	Davenport, Iowa	Big 4 Wonders Indian Remedies; Spirit Lake Salts; Big 4 Wonders Iron Tonic; Black Bath Mineral; X X White, Mineral; Stomach Capsules; Vaginal Suppositories; Mineral Laxatives	Dec. 4, 1939	13576

TABLE 2.—*Résumé of Fraudulent "Cure-Alls," Referred to in This Article*

	Diseases for Which the Remedies Were to Be Used																
Name of the Promoter of the Remedies	Apparently Any Ailment or Disorder	Asthma	Anemia	Bladder Diseases	Cancer	Diabetes	Eye Diseases	Female Disorders	Hemorrhoids	High Blood Pressure	Kidney Diseases	Malaria	Piles	Pyorrhea	Rheumatism	Sores	Stomach Troubles	Other Conditions Specifically Mentioned in the Advertisements
Arrowhead Indian Herbs....	X																	
Botanical Medicine Co.....	..	..	X	X	..	X	X	X	X	X	X	..	X	X	X	X	X	Gallbladder troubles, gallstones
Crocker's Asthma and Lung Trouble Medicine Co.	..	X	..	..	X	X	..	..	..	X	..	..	..	..	..	..	..	Diphtheria, dropsy, lung trouble, loss of manhood, menopause
H. W. Lange & Son.....	..	..	X	..	..	..	X	X	..	..	..	..	..	..	X	..	..	Abscesses, adenoids, bronchitis, diarrhea, earache, leukorrhea, delayed and painful menstruation, nasal catarrh, nervousness, neuritis, ovary troubles, tonsils, falling womb
Morehead & Co.....	X	X	X	X	..	X	..	X	X	X	X	X	X	..	X	..	X	Loss of hearing, gallstones, gastritis, skin diseases, running sores, all tumors
Prof. C. A. Isbell.....	..	..	..	..	X	X	..	..	..	..	..	..	X	X	X	X	X	Blood purifier, constipation, eczema, "social" diseases
Theodore M. Moore.....	X	X	..	X	X	X	..	X	X	X	X	X	X	..	X	..	..	Deafness, failing eyesight, paralysis, sleeping sickness, tuberculosis, insanity, syphilis

Correspondence

SERUM CENTER IN IOWA

To the Editor:—My attention has been called to an item in THE JOURNAL of August 10 under Queries and Minor Notes, page 480, on convalescent serum for contagious diseases. In referring to sources of convalescent serum the State of Iowa Department of Health is not mentioned.

I therefore wish to add that in 1937 the State of Iowa Department of Health organized its serum center for the processing of human immune serum. Since its organization the Serum Center has distributed a total of 213,000 cc. of human serum. Of this amount 23,655 cc. has been distributed for measles, 135,490 cc. for scarlet fever and 42,980 cc. for poliomyelitis. Lesser amounts have been processed for Rocky Mountain spotted fever, pertussis and tularemia. The convalscent serum is sent to licensed physicians on request without charge. When the economic status of the patient permits, a contribution is accepted to the donor's fund. Donors are paid $5 for 250 cc. of blood. The attending physician is expected to send a complete clinical report of all cases in which the convalescent serum is used. The serum center is at present also processing human serum for transfusion purposes in accordance with the procedure of Carlson and Levinson. The State of Iowa Department of Health is the one state department at the present time processing convalescent serum.

The Serum Center was properly licensed by the Federal Security Agency, National Health Institute, Division of Biologics Control in September 1939. At that time the license granted interstate traffic to measles, scarlet fever and poliomyelitis human immune serum and normal human serum. Later, in May 1940, the license was extended to include pertussis immune serum.

WALTER L. BIERRING, M.D., Des Moines, Iowa.
Commissioner, State of Iowa Department of Health.

HEALTH SERVICE SYSTEM OF SAN FRANCISCO

To the Editor:—In THE JOURNAL (August 17, p. 540) under the heading Organization Section, you carry an article on the health service system of San Francisco.

Your readers should know that the statements and statistics in this article are taken from a pamphlet prepared by the lay board that operates the system. The physicians who actually perform the services under the system (over 95 per cent of whom are members of the San Francisco County Medical Society) presented an analysis of the report in the May 1940 issue of the *Bulletin of the San Francisco County Medical Society.*

It is important for your readers to note that the chief complaint of the physicians has not been that the value of the unit was too low. It has been that the system has been conducted in an arbitrary manner, with very slight attempts on the part of the director to cooperate with the county medical society. The official manager's report conceals the fact that in 1939 the physicians actually contributed more than $132,000 worth of medical services without remuneration, this sum being based on the modest schedule in effect during that year. It is readily admitted that the employees called for an unreasonably large amount of medical service. Nevertheless, if the visits and services actually made (but arbitrarily disallowed) were included in the computation of the unit paid, it would reveal the fact that the doctors were paid about 50 cents on the dollar.

The physicians of San Francisco are happy to cooperate with any constructive voluntary health insurance system in the operation of which they have a proper voice. They do believe, however, that the true facts should be known, since faulty conclusions could easily be drawn from the figures you publish.

L. HENRY GARLAND, M.D., San Francisco.
Secretary, San Francisco County Medical Society.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

"METAL FUME FEVER" IN WELDERS

To the Editor:—My attention has been called to a condition of vertigo, profuse perspiration, dyspnea and rapid pulse suffered by men using the electric welding apparatus on galvanized material at the Pearl Harbor Navy Yard. Recently several patients have consulted me primarily for a nasal congestion and a wet nose together with some vertigo and ocular instability. They all gave the history of having worked either as an electric welder or in close connection with this kind of work. I am wondering if there is a possibility that these patients are suffering from a poisonous effect from the gas generated by such a job. Have you anything in your files concerning this type of poisonous gas and if so would you please send me a digest of it or tell me where it can be found?

M.D., Honolulu, T. H.

ANSWER.—A considerable number of cases of metal fume fever have been reported in past years among welders engaged in the welding or cutting of galvanized steel in naval vessels, particularly in confined spaces. The condition now is comparatively infrequent owing to the efficiency of the protective measures which have been introduced.

The galvanized coating is basically zinc and contains from 95 to 96.5 per cent of that metal. It also contains from 0.75 to 1 per cent of lead and from 2.5 to 4 per cent of iron. Metal fume fever results from the inhalation of zinc oxide fumes incident to the welding or the cutting of the metal, lead being present in such traces as to be apparently negligible.

Metal fume fever has long been recognized as an industrial disease. Other terms commonly applied to the condition are brass founders' ague, brass chills and zinc fever. At one time it was of common occurrence among brass foundry and zinc smelting workers. Generally attacks today are found as a result of welding or cutting of galvanized sheets and pipes.

It is an acute, transitory, nonfatal disease causing slight or temporary disability. A strict interpretation of the term metal fume fever does not place it in the class of conditions termed metal poisoning. The reaction set up in the body is not directly ascribed to the toxic metal or dependent on the inherent toxicity of the metal particles inhaled. The superficial action of the inhaled finely divided zinc oxide injures the epithelial cells lining the respiratory tract. The absorption of the altered proteins of these cells affects the individual much the same as the typhoid inoculation or the injection of other foreign protein.

At the end of the day, or from two to twelve hours following exposure to the zinc fumes, the worker notices a dryness of the throat in addition to a metallic taste which most workers commonly report during exposure. There is usually a feeling of tightness of the chest, varying with the exposure. This tends to indicate the severity of chills and fever which are to follow. Occasionally nausea and vomiting occur. When mildly affected the patient may not be aware of any fever and complain only of a chilly sensation followed by sweating and general weakness. Exposure to extreme cold may hasten the onset of the fever and chills, but as a rule the worker awakens from sleep with a high temperature and chills, which are quite similar to the chills and fever experienced in attacks of malaria. Toward the end of the attack the individual sweats profusely and is left with a feeling of weakness. In the majority of cases some weakness is still felt the next day. The time loss, however, is rarely beyond one day.

Metal fume fever may sometimes be overlooked unless the physician considers the occupational environment. It may simulate attacks of grip or bronchitis or, if in a malarial region, it may be mistaken for an attack of malaria. Continued work

produces an immunity or raises resistance, but this is lost after a layoff from work.

There appears to be no conclusive evidence that chronic effects are produced by repeated exposure to zinc fumes.

The prevention of metal fume fever in welding is accomplished in naval vessels by means of localized exhaust, the fumes being removed at the source. A light metal pipe approximately 3½ inches in diameter connected to an exhaust blower serves to remove the bulk of the zinc fumes at the line of the weld. This is carried along with the work from place to place. In addition, respirators are provided for special protection under unusual circumstances. Ordinarily the localized exhaust, if used in compliance with instructions, is adequate to prevent metal fume poisoning.

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ULTRAVIOLET RAYS FOR AIR STERILIZATION IN AIR CONDITIONING SYSTEMS

To the Editor:—**There has been considerable discussion concerning the use of ultraviolet rays in air conditioning systems for sterilizing the air, particularly because in many systems in which the air is cooled approximately 75 per cent is recirculated from the cooled space, with the possibility that it might carry bacteria. Ultraviolet rays, if used, would be introduced into the recirculated air path, where the velocity may be as high as 1,000 feet per minute. There is a question as to whether such an arrangement would be effective and also a question as to the results that might be accomplished with ultraviolet rays even though the velocity of the air passing the ultraviolet source is not so great. Any information you can supply concerning this matter would be appreciated.**

M.D., Wisconsin.

ANSWER.—Wells, investigator of air-borne bacteria and ultraviolet rays for bactericidal purposes, in a recent publication (*J. Franklin Inst.* **229**:347 [March] 1940) provides much information dealing with the points raised in this query. In a smooth tunnel 100 feet long, the other dimensions being 7 by 8 feet, a standard ultraviolet lamp was set up near the center. At the air entry end of the tunnel, Escherichia coli cultures were sprayed into the atmosphere. Various determinations were made as to the killing action of ultraviolet emanations under various conditions, including velocity, humidity and nearness to the lamp. At a velocity of 222 feet per minute and a relative humidity of 43 per cent, when the bacterial count prior to ultraviolet action was 1,250 per sample, a drop to 303 bacteria occurred after passing the rays. At a velocity of 21 feet and a relative humidity of 67 per cent, the count before exposure of 42,000 bacteria dropped to 12,500 after action of the rays.

In another publication (*Am. J. Pub. Health* **29**:863 [Aug.] 1939) Wells and his associates report some bacterial counts made in an air conditioned railway car with and without the action of ultraviolet rays in the air conditioning. On this car the passenger load varied from one to sixty-nine. With the ultraviolet rays turned off and a passenger load of one, the total bacteria count was 232. When the passenger load was sixty-nine the bacterial count was 1,324. When the ultraviolet rays were operating, at a time when the passenger load was fifteen, the lowest reported in this particular series of experiments, the bacteria count was 349, the highest count in this series of samples. When, however, the passenger load was fifty-five the bacterial count was in one sample 186, the lowest figure associated with any passenger load.

From all experimental work, several complex formulas have been devised permitting computations under varying circumstances as to intensity of radiation, air velocity, type of air flow, distance from the rays and the like. The mere introduction of ultraviolet units in the conduits of an air conditioning system affords no assurance of extensive bactericidal action. Conversely, full consideration for all factors involved might indicate sets of ultraviolet radiating facilities sufficient to cope with any air velocity and bacterial load. The practicability of such equipment under some circumstances is open to debate. Nothing in the publications of Wells as cited suggests that with an assumed velocity of 1,000 linear feet per minute a near-sterile air may be obtained. On the other hand, it is to be recognized that suitable intensities and suitable distribution of ultraviolet lamps in connection with air conditioning will effect some reduction in atmospheric bacterial contamination.

DERMATALGIA

To the Editor:—**A woman aged 83, usually in good health, three months ago developed intertrigo between her thighs. This healed with slight medication. Six weeks later her feet at night became uncomfortable because of warmth heat. I do not find this discussed in available textbooks. Nothing I have prescribed has been of benefit. She is compelled to sleep with her feet exposed. She is kept awake from two to four hours each night. Her discomfort is distressing. The patient is a college graduate and is not neurotic or unusually sensitive. I have tried many lotions and the like and have consulted with my medical friends. I do not find the condition discussed in medical books available.**

M.D., New Jersey.

ANSWER.—From the description it is assumed that there is no change in the appearance of the skin during attacks, thus justifying the diagnosis of dermatalgia, a disturbance of the nerves supplying the skin of the part affected, supposedly the nerves of the vegetative system. The pain varies in different cases, burning as in the case cited, or a sensation of hot or cold water running over the skin, of stabbing, cutting, rubbing of the skin, or the sensation of an electric current. The attacks come on usually at night, affect middle aged women most often and are commonly associated with hyperesthesia so that the contact of clothing or other objects adds to the distress. Hairy parts or the extremities are most often involved.

This disease was discussed in answer to a query on page 739 of THE JOURNAL, Aug. 31, 1935. As possible etiologic factors tabes dorsalis, malaria, rheumatism, diabetes mellitus, leukemia and other members of the lymphoblastoma group and leprosy were mentioned. In addition chlorosis, hysteria and any cause of neuritis are mentioned in the literature. Exposure to cold is also mentioned, probably the reason for the mention of rheumatism. It might be well to examine for anemia and the possibility of certain forms of avitaminosis, especially those in which elements of the vitamin B complex are concerned.

If any such cause can be discovered, treatment directed accordingly may succeed in eradicating the pain. If not and in the considerable proportion of the cases in which no such basis can be found, acetylsalicylic acid, salicin, quinine and arsenic are recommended and the local use of alternating hot and cold applications, galvanic or faradic electricity, or counterirritation over the nerves supplying the part. Langeron and Desplats are quoted as having suggested roentgen therapy over the sympathetic centers for the relief of the pain of dermatalgia. The reference given in the article on dermalgie in the Nouvelle pratique dermatologique, volume 5, page 759, is incorrect and the article of Langeron and Desplats has not been traced. A small dose of roentgen rays, from 40 to 80 roentgens filtered through 2 mm. of aluminum, may be effective. This can be repeated at weekly intervals.

As advised in the query of 1935, the skin should be protected as well as possible from the irritation of clothing.

LEAD IN INSULATING MATERIAL

To the Editor:—**Have you any information concerning the possibility of lead poisoning to the occupants of a house which is insulated by a material made by the Eagle Picher Company. This material is made from lead slag as a base and is a by-product of the refinement of lead ore. There might be slight sifting through plaster cracks and if the material is not entirely inert there might be an appreciable danger.**

George B. Stericker, M.D., Springfield, Ill.

ANSWER.—The chemical composition of Eagle Mineral Wool Home Insulation has been supplied by the firm as follows:

Iron silicate	54.82%
Aluminum silicate	7.40
Calcium silicate	24.23
Magnesium silicate	3.39
Lead silicate	.61
Manganese silicate	.57
Zinc oxide	9.46
	100.48%

While the constituents listed total more than 100 per cent, the excess may be charged to experimental error. It should be noted that most of the constituents in this mineral wool are in the form of silicates and the trace of lead silicate present is highly insoluble and is regularly used as a constituent of high grade tableware. The possibility of lead poisoning from this

source is rather remote because of the small proportion of lead in the material and the small amount of insulation which might seep through cracks in the plaster. Although this situation does illustrate another potential lead exposure of the general population, the insulation in question with its present chemical constituents has been manufactured and sold in large quantities for more than ten years without knowledge on the part of the manufacturers of a single case (including those handling the installation contracts) of any form of illness or disease resulting from the material.

CHRONIC SAPHENOUS PHLEBITIS AND POSSIBLE EMBOLISM

To the Editor:—On March 7, 1940, a married woman aged 46 developed a sudden pain in the right chest. I examined her chest and found no gross abnormality and made a diagnosis of acute pleurisy. Four hours later I reexamined the patient and discovered an area of consolidation involving the right middle lobe. A variety of râles were present. She coughed and expectorated some bloody sputum. The pulse rate was 130 and the temperature was 100 F. I made a provisional diagnosis of pneumonia. At the hospital the white count was 14,000. A few of the higher type pneumococci were found in the sputum. X-ray examination revealed irregular consolidation of the entire right lung suggesting pneumonia. This cleared in about ten days both clinically and roentgenologically with no specific medication. The temperature ranged between 100 and 101 F. for a week. Nine months previously she had cardiac arrhythmia and she complained about dyspnea. This led a colleague and me to think about the possibility of a pulmonary embolus. She was given only digitalis and morphine. About one week after the onset of the illness phlebitis of the first saphenous vein above the thigh was noted. It was then thought that an embolus developed from this site, although the patient did not complain until later. One consultant felt that the phlebitis was secondary to a pneumonia. On March 20 the patient was discharged apparently well. The pulse rate was 90. There was no fever, and pain in the leg was slight. On March 27, after an attack of coryza, there was a recurrence of the phlebitis. The temperature varied between 99 and 100 F. The average is 99.6 F., in the afternoon and has continued so for nearly four months. The first saphenous vein is painful and tender and feels beaded on palpation. The pulse rate remains at 90. The chest appears clear and there are no chest symptoms. The leg is not swollen and has never been swollen. The patient has been in bed since the onset of her illness. A patch tuberculin test was negative. This was done because of a positive history of tuberculosis in the family. Sputum tests were negative for acid fast organisms. Urinalysis and blood chemistry were normal. The blood Wassermann reaction was negative. X-ray examination of the chest was not repeated because I have feared to have her get out of bed because of the possibility of embolism. My patient has become quite discouraged because there has been no improvement with prolonged rest. I told her that she would be permitted to get up after the temperature remained normal for a time. I hesitate to allow her out of bed because of the possibility of embolism and the possibility of aggravating the inflammation. Treatment has been conservative. Moist and dry heat have been applied locally to the veins. Is this an unusual duration of fever with phlebitis? How long can I expect this fever to continue? What can be done to shorten the course of the inflammation? Would I be justified in using foreign protein therapy?

Joseph F. Lechman, M.D., Latrobe, Pa.

ANSWER.—The description of the initial attack may well fit the picture of pulmonary embolism but the origin of the embolus is obscure. One would have to know whether a pelvic phlebitis is present, which often accompanies infections of the female genitals. A previous history of pain and swelling following childbirth or operation might give a hint as to the existence of a latent pelvic thrombosis. The existence of varicosities is not mentioned in the query. The fact that a saphenous phlebitis followed instead of having preceded the suspected infarct is not unusual, as short clots in the external or internal iliac veins often show a retrograde extension into the veins of the lower extremities after the appearance of the infarct.

Phlebitis following pneumonia is, of course, an equally good possibility; however, it usually appears in a form of an iliofemoral phlebitis causing swelling, discoloration and visible distention of the superficial veins.

The following methods of treatment are worthy of consideration: (1) eradication of all foci of infection, especially in the teeth and tonsils, (2) small doses of roentgen rays (100 roentgens with heavy filter) at weekly intervals, (3) small doses (from 2 to 2.6 Gm.) of sulfanilamide for from ten days to two weeks. The virulence of the process can be gaged best by the sedimentation rate. If this is a true saphenous phlebitis without involvement of the deep veins there is no need to keep the patient immobilized; the saphenous vein can be tied at its junction with the femoral, thus excluding a possible source of emboli. The division of the vein often hastens the subsidence of phlebitis. If the coagulation time is too short, heparin or leeches are often helpful. The decision as to when to let the patient get up and which of the methods mentioned should be employed requires considerable clinical experience. Recurrent phlebitis and embolism may occur as late as eight years after the initial attack.

A PATENTED ORAL TREATMENT FOR HAY FEVER

To the Editor:—I have heard something about a pollen mixture in yeast of bread making for treatment of hay fever. It was stated that such a patent was given to a Kurt Rosenwald of New York. Could you give me any information on this method?

Leslie S. Harrison, M.D., Bayside, N. Y.

ANSWER.—U. S. Patent 2,207,415, issued July 9, 1940, to Kurt Rosenwald of New York, is described as "the peroral treatment of hay fever in a therapeutical preparation, in which the principal effecting ingredient is a decomposition product of the protein of the pollen of at least one hay-fever-causing plant to which the patient is sensitive, said decomposition product being formed by the action of yeast on said pollen." Apparently this claim of therapy in hay fever is based on the supposition that a digestion product of the pollen taken by mouth will produce some form of immunization. The inventor adds yeast and pollen to a food or drink, such as bread dough, grape juice or beer. In some respects this treatment resembles that proposed a number of years ago by Urbach, in which propeptones of pollen were administered. Since oral pollen therapy has been found to have little if any effectiveness, since Urbach's propeptones have been virtually discarded, at least in this country, and since the proteolytic action of yeast cannot be expected to be more effective than the proteolytic action of the gastrointestinal enzymes, it is difficult to understand how such therapy can be expected to operate.

FATTY DEGENERATION AND INFILTRATION OF HEART

To the Editor:—In Modern Concepts of Cardiovascular Disease (published by the American Heart Association), in volume 7, No. 9 (Sept.) 1938, appears the following statement: "When excess deposits of fat occur in the subpericardial space, penetration or infiltration of fat into the connective tissues lying between the muscle bundles occurs, and at times the penetration occurs between the individual muscle fibers but not into the muscle cell." In an article by E. Perry McCullagh of Cleveland (Management of Obesity, *Ohio State M. J.* 34:1131 [Oct.] 1938), under Clinical Manifestations, the following statement appears: "The heart may be embarrassed for several reasons. It is encroached upon by fat either about the heart, between the muscle fibers, or in the cells themselves." Which view is correct?

Richard P. Shapiro, M.D., Philadelphia.

ANSWER.—Fatty infiltration between the heart muscle bundles is a common observation, especially in the obese, as in middle aged and elderly women, particularly involving the right ventricle; but fat in the muscle cells themselves occurs only in strictly disease conditions in which there is degeneration of the cells, as in the first stages of infarction or other serious involvement of the myocardium per se. Of course it is possible to have both fatty infiltration and fatty degeneration in the same patient, but either may occur alone.

SENSITIVITY TO LIVER PREPARATIONS

To the Editor:—A woman aged 38 suffering from primary anemia has been under treatment for ten years, recently taking an oral preparation which has maintained her blood picture essentially normal, other than for minor poikilocytosis, and has kept her entirely free from symptoms. The cost of this preparation, however, is considerable—about $15 every six weeks—and this works a definite hardship on her. She has tried raw liver and numerous other preparations containing liver, but nausea prevents therapy other than in capsule form orally. There is a history of the use of parenteral liver therapy about eight years ago, but reactions were so severe that she had to give up this form of therapy. I have recently started treatment with a concentrated liver solution containing 10 U. S. P. units per cubic centimeter. Three injections at weekly intervals caused no untoward response, but the fourth brought forth a typical allergic phenomenon with urticaria and circumoral and circumorbicular flushing and edema. This reaction lasted about twenty-four hours and then subsided. The next parenteral injection is due next week, and I intend changing to a more refined preparation of 15 U. S. P. units per cubic centimeter. If the reaction still occurs, which is the better course of procedure—to change back to oral liver, which I am reluctant to do, to administer liver therapy with ephedrine sulfate and a barbituric acid derivative parenterally or to try desensitization. If the latter, how may it be carried out and, if once desensitized, will sensitivity redevelop in the intervals between weekly injections?

M.D., Massachusetts.

ANSWER.—Allergy to liver extract in a patient with pernicious anemia is a distressing and sometimes serious situation. Parenteral extract of several different manufacturers might be tried first. It is usually possible to find a preparation to which the patient is not sensitive. It is well to use the most concentrated extracts available, with the hope that the antigenic substance has been eliminated by refining. Trying to give a liver extract to which the patient is known to be sensitive and then attempting to control the reaction with drugs is not advised. Desensitization is not often successful. If a preparation cannot be found to which the patient is not allergic, oral therapy should be continued.

MORPHINE AND PARALDEHYDE

To the Editor:—Have you any information on synergistic toxicity in the use of paraldehyde and morphine? A recent article in a trade publication mentioned that the use of these drugs together may produce serious results.

M.D., Virginia.

ANSWER.—A search of the literature has failed to show any work which would confirm the statement that paraldehyde and morphine when used simultaneously have a synergistic toxicity. One of the widely used methods of controlling eclampsia consists in the intravenous administration of paraldehyde and at the same time the hypodermic use of from one-fourth to one-half grain (0.016 to 0.032 Gm.) of morphine sulfate.

Paraldehyde in therapeutic doses does not depress the heart or respiration. In many cases it seems to exert a stimulating action.

POSSIBLE SENSITIZATION TO DIGITALIS

To the Editor:—Can the human body occasionally become sensitized to digitalis? In August 1939 I gave an excess of digitalis to a 64 year old woman with the usual after-symptoms of overdosage. Later, with the advice of a good cardiologist, I gave one-third tablet of gitalin daily for months. In April of this year I gave her 9 grains (0.6 Gm.) of standard digitalis within twenty-four hours, thinking I saw indications. She had an extreme gastric upset which lasted to some degree for ten days. I then stopped all medication and continued bed rest for thirty days and started the gitalin, one-third tablet daily. The second third of a tablet was followed by gastric pain occurring six or eight hours after and lasting two or three hours with definite fall of pulse rate (from 85 to 55 and 60) and gastric upset. I am inclined to feel that she was suffering from the two small doses and is therefore sensitized to digitalis and its preparations.

J. D. Michie, M.D., Childress, Texas.

ANSWER.—While it is unwise to say that certain things never happen in the field of medicine, especially in allergy, a careful perusal of the literature shows no reference to allergic intolerance of digitalis. The following works, limited to digitalis, fail to mention this as a possibility: Hefftner, A.: Handbuch der experimentellen Pharmakologie, Berlin, Julius Springer, 1935, vol. 1; Weese, H.: Digitalis, Leipzig, Georg Thieme, 1936. Nor does a general manual of pharmacology, like that by Sollmann (fifth edition, 1936), mention this as a possibility. It seems probable from the history given that the reaction described is not allergic.

PROSTIGMINE COMPOUNDS AND GLAUCOMA

To the Editor:—A patient is being treated for moderate glaucoma with drops of pilocarpine solution. She has some ear trouble (blocking of eustachian tubes) and the otologist prescribed prostigmine bromide 15 mg. three times a day and prostigmine methylsulfate (1:2,000) by injection twice weekly. Will this treatment be detrimental or have any effect on the eye? The otologist does not want to give an opinion. Will this treatment have any effect on the eye muscles as in myasthenia gravis?

B. O. LeBlanc, M.D., St. Gabriel, La.

ANSWER.—The preparations of prostigmine mentioned would not have any detrimental effect on the eye. It is even possible that they might have a beneficial effect in the case of glaucoma, although this is certainly doubtful. Prostigmine compounds are, of course, closely related to those of physostigmine and are used in the form of drops as a substitute in some cases of glaucoma.

DISCHARGING BREAST

To the Editor:—A woman aged 46 has one breast that has been discharging a thin yellowish to a fairly thick yellowish serous fluid for the past ten or eleven years, since her last child was born. One year ago this breast discharged a light bloody fluid for about two weeks, then a dark bloody fluid for two weeks and thereafter the serous fluid again. Recently the bloody discharge has begun again. There are no masses, no induration, no shadows on transillumination, no pain and no tenderness. Estrogen has been given without any noticeable result. I am especially interested to know whether there would be any value in administering 1:4,000 prostigmine methylsulfate solution in an attempt to clear up the discharge from a breast which gives absolutely no shadow of any kind on careful transillumination.

M.D., Texas.

ANSWER.—In view of the long-standing history and the completely negative physical examination, one is inclined to assume that at present a malignant condition is not apparent, although it might be microscopic. It is difficult to understand how prostigmine methylsulfate solution could inhibit the discharge. Possibly testosterone propionate might be of benefit, at least temporarily, by causing involution of the breasts. Twenty-five mg. of testosterone propionate, in such instances, is injected subcutaneously three times a week for a period of from four to six weeks. The danger of producing virilism, such as hirsutism, change in voice and enlargement of the clitoris, cannot be overlooked. However, the suggested dose is not large and the risk is probably slight. Furthermore, signs of virilism practically always disappear when the drug is discontinued. The discharge may stop spontaneously when the ovaries cease to function. If testosterone propionate does not inhibit the discharge, radiation therapy to the ovaries may be considered. There is not likely to be harm in this procedure because the patient is 46 years old.

ONYCHOGRYPHOSIS

To the Editor:—A man aged 44 has onychogryphosis. He is a produce merchant in a vegetable market. The nails affected are those of the two index fingers and the condition seems to be directly attributable to the constant lifting of cases of iceberg lettuce by the use of both index fingers. It has had a gradual onset for six weeks. For three weeks I pared the thickened nails down to the matrix, applied a 3 per cent salicylic acid ointment, used warm soaks, and now am trying to restore the nutrition of the nail and fingers with diathermy. The literature gives a paucity of information concerning its cure. I have been unable to cure his condition. Could you please give me the latest opinions as to etiology and effective therapy in onychogryphosis.

Vincent J. Barone, M.D., Elmhurst, Queens, N. Y.

ANSWER.—In onychogryphosis the nail becomes enormously thickened and clawlike. Pressure, warmth and lack of proper care are contributing causes. Thickened and enlarged nails are at times observed in leprosy, tuberculosis, acromegaly and syringomyelia. The hypertrophic changes may often be found in association with local irritation or injury and with gout, rheumatism and certain diseases, e. g. eczema, paronychia, psoriasis and occupational dermatitis.

It is suggested that trauma be avoided as far as possible; the patient might consider wearing canvas gloves at his work, and careful cleanliness and regular manicure of nails should be insisted on.

An unusual case of onychogryphosis on the basis of a combination of rheumatism and lack of care in a patient aged 73 was reported by Wien and Perlstein (*Arch. Dermat. & Syph.* **28**:807 [Dec.] 1933).

POSSIBLE HOMOSEXUAL TENDENCIES

To the Editor:—A man whose standing, personally and professionally, has always been beyond reproach or question has been accused of improper sex relations with other men, these men stating that he approached them not by question but by touch. It has been established that the men in question are of somewhat doubtful character and one of them, at least, has reason to wish this man harm. The man's personal life is far above the average; he has a wife and children and is splendidly educated. I cannot find it possible to believe such accusations. He has denied them and was shocked beyond belief at having them made. He is perfectly willing to undergo any examination, physical or psychologic, which would assist in proving him innocent or incapable of such conduct. The problem presented is What examinations? I have never before been confronted with such a matter, have no literature dealing with it and am at a total loss as to procedure. This matter is vitally important to this man's career.

M.D., Florida.

ANSWER.—The patient should be given a complete medical and psychiatric examination. Any standard textbook of psychiatry outlines the routine psychiatric form to be followed. The following textbooks are suggested:

Henderson, D. K., and Gillespie, R. D.: A Textbook of Psychiatry, ed. 4, New York, Oxford University Press, 1938.

Singer, H. D., and Krohn, W. O.: Insanity and Law, Philadelphia, P. Blakiston's Sons & Co., 1924.

The problem in this case may be one of homosexual tendencies in an otherwise normal person. It is well known that such homosexual tendencies are merely arrests in psychologic development and that such people may marry and have a perfectly happy family life but may continue to exhibit homosexual interests. They require prolonged psychotherapeutic help and should be under the direct care of a psychiatrist. Many of them can be helped, but, more important, they must be protected from hostile and often trouble-making persons in their environment.

CHRONIC NODULAR PHLEBITIS

To the Editor:—A patient has a series of small nodules within the walls of the brachial vein and its branches in the forearm. They are accompanied by numbness in the forearm. The patient is a man aged 32 and has always been well. The Wassermann reaction is negative. What might these small hard nodules be?

C. W. Henney, M.D., Portage, Wis.

ANSWER.—The syndrome of chronic nodular phlebitis has been described by Gougerot. It may be due to low grade pyogenic, tuberculous, syphilitic or mycotic infection. The nodules may form sharp edged, poorly granulating ulcers with a yellowish base. There is no fever or glandular involvement. When seen early the granuloma is under the intima and may resemble a rheumatic nodule. In this particular case, because of the associated numbness, one should think of the possibility of a neurofibromatosis of Recklinghausen originating from the sheaths of peripheral nerves.

Medical Examinations and Licensure

COMING EXAMINATIONS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and Examining Boards in Specialties were published in THE JOURNAL, September 21, page 1043.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: Montgomery, June 17-19. Sec., Dr. J. N. Baker, 519 Dexter Ave., Montgomery.

ARIZONA: * *Written.* Phoenix, Oct. 1. *Reciprocity.* Phoenix, Oct. 2. Sec., Dr. J. H. Patterson, 326 Security Bldg., Phoenix.

ARKANSAS: * *Regular.* Little Rock, Nov. 7-8. Sec., Dr. D. L. Owens, Harrison. *Eclectic.* Little Rock, Nov. 7. Sec., Dr. Clarence H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Oral examination* (required when reciprocity application is based on a state certificate or license issued ten or more years before filing application in California), San Francisco, Oct. 2. *Written examination.* Sacramento, Oct. 21-24. Sec., Dr. Charles B. Pinkham, 1020 N St., Sacramento.

CONNECTICUT: * *Written.* Hartford, Nov. 12-13. *Endorsement.* Hartford, Nov. 26. Sec., Dr. Thomas P. Murdock, 147 W. Main St., Meriden. *Homeopathic.* Derby, Nov. 12-13. Sec., Dr. Joseph H. Evans, 1488 Chapel St., New Haven.

DELAWARE: July 8-10. Sec., Medical Council of Delaware, Dr. Joseph S. McDaniel, 229 S. State St., Dover.

DISTRICT OF COLUMBIA: * Washington, Nov. 11-12. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: * Tampa, Nov. 18-19. Sec., Dr. W. M. Rowlett, Box 786, Tampa.

GEORGIA: Atlanta, Oct. 8-9. Joint-Sec., State Examining Boards, Mr. R. C. Coleman, 111 State Capitol, Atlanta.

HAWAII: Honolulu, Jan. 8-11. Sec., Dr. James A. Morgan, 48 Young Building, Honolulu.

IDAHO: Boise, Oct. 1. Dir., Bureau of Occupational License, Mr. H. B. Whittlesey, 355 State Capitol Bldg., Boise.

ILLINOIS: Chicago, Oct. 1-3. Superintendent of Registration, Mr. Lucien A. File, Springfield.

INDIANA: Indianapolis, June 17-19. Sec., Board of Medical Registration and Examination, Dr. J. W. Bowers, Citizens Trust Bldg., Fort Wayne.

KANSAS: Topeka, Dec. 10-11. Sec., Dr. J. F. Hassig, 905 N. Seventh St., Kansas City.

KENTUCKY: Louisville, Dec. 3-5. Sec., State Board of Health, Dr. A. T. McCormack, 620 Third St., Louisville.

MAINE: Portland, Nov. 12-13. Sec., Board of Registration of Medicine, Dr. Adam P. Leighton, 192 State St., Portland.

MARYLAND: *Regular.* Baltimore, Dec. 10-13. Sec., Dr. John T. O'Mara, 1215 Cathedral St., Baltimore. *Homeopathic.* Baltimore, Dec. 10-11. Sec., Dr. John A. Evans, 612 W. 40th St., Baltimore.

MASSACHUSETTS: Boston, Nov. 12-14. Sec., Board of Registration in Medicine, Dr. Stephen Rushmore, 413-F State House, Boston.

MICHIGAN: * Lansing, Oct. 9-11. Sec., Dr. J. Earl McIntyre, 202-4 Hollister Bldg., Lansing.

MINNESOTA: * Minneapolis, Oct. 15-17. Sec., Dr. Julian F. Du Bois, 350 St. Peter St., St. Paul.

MISSISSIPPI: *Reciprocity.* Jackson, December. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MISSOURI: Kansas City, Oct. 29-31. Sec., State Board of Health, Dr. Harry F. Parker, State Capitol Bldg., Jefferson City.

MONTANA: *Reciprocity.* Helena, Sept. 30. *Written.* Helena, Oct. 1-2. Sec., Dr. S. A. Cooney, 216 Power Block, Helena.

NEVADA: Reciprocity with oral examination, Nov. 4. Sec., Dr. Fred M. Anderson, 215 N. Carson St., Carson City.

NEW HAMPSHIRE: Concord, March 13-14. Sec., Board of Registration in Medicine, Dr. T. P. Burroughs, State House, Concord.

NEW JERSEY: Trenton, Oct. 15-16. Sec., Dr. Earl S. Hallinger, 28 W. State St., Trenton.

NEW MEXICO: Santa Fe, Oct. 7-8. Sec., Dr. Le Grand Ward, 135 Sena Plaza, Santa Fe.

NORTH CAROLINA: *Reciprocity.* Durham, Dec. 3. Sec., Dr. W. D. James, Hamlet.

NORTH DAKOTA: Grand Forks, Jan. 7-10. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OKLAHOMA: * Oklahoma City, Dec. 11. Sec., Dr. James D. Osborn Jr., Frederick.

OREGON: * *Reciprocity.* Portland, October. *Written.* Portland, Jan. 14-16. Exec. Sec., Miss Lorienne M. Conlee, 608 Failing Bldg., Portland.

PENNSYLVANIA: Philadelphia, January. Acting Sec., Bureau of Professional Licensing, Miss Marguerite G. Steiner, 358 Education Bldg., Harrisburg.

RHODE ISLAND: * Providence, Oct. 3-4. Sec., Division of Examiners, Dr. Robert M. Lord, 366 State Office Bldg., Providence.

SOUTH CAROLINA: Columbia, Nov. 12. Sec., Dr. A. Earle Boozer, 505 Saluda Ave., Columbia.

SOUTH DAKOTA: * Pierre, Jan. 21-22. Dir., Medical Licensure, Dr. J. F. D. Cook, Pierre.

TEXAS: Austin, Nov. 25-27. Sec., Dr. T. J. Crowe, 918-920 Mercantile Bldg., Dallas.

VERMONT: Burlington, Feb. 11. Sec., Dr. W. Scott Nay, Underhill.

VIRGINIA: Richmond, Dec. 4-6. Sec., Dr. J. W. Preston, 30½ Franklin Rd., Roanoke.

WEST VIRGINIA: Morgantown, Oct. 31-Nov. 2. Sec., Public Health Council, Dr. Arthur E. McClue, State Capitol, Charleston.

WISCONSIN: * Madison, Jan. 14-17. Sec., Dr. H. W. Shutter, 425 E. Wisconsin Ave., Milwaukee.

WYOMING: Cheyenne, October. Sec., Dr. M. C. Keith, Capitol Building, Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

CONNECTICUT: New Haven, Oct. 12. Address State Board of Healing Arts, 1945 Yale Station, New Haven.

DISTRICT OF COLUMBIA: Washington, Oct. 21-22. Sec., Commission on Licensure, Dr. George C. Ruhland, 203 District Bldg., Washington.

FLORIDA: Gainesville, Nov. 1. *Applications must be on file not later than Oct. 16.* Sec., Prof. J. F. Conn, John B. Stetson University, DeLand.

IOWA: Des Moines, Oct. 8. Dir., Division of Licensure and Registration, Mr. H. W. Grefe, Capitol Bldg., Des Moines.

MINNESOTA: Minneapolis, Oct. 1-2. Sec., Dr. J. Charnley McKinley, 126 Millard Hall, University of Minnesota, Minneapolis.

NEBRASKA: Lincoln, Oct. 1-2. Dir., Bureau of Examining Boards, Mrs. Clark Perkins, 1009 State Capitol Bldg., Lincoln.

OKLAHOMA: Oklahoma City, Nov. 18. Sec., Dr. James D. Osborn Jr., Frederick.

OREGON: Portland, Oct. 26. Sec., Mr. Charles D. Bryne, State Board of Higher Education, University of Oregon, Eugene.

RHODE ISLAND: Providence, Nov. 20. Acting Chief, Division of Examiners, Mr. E. Clyde Thomas, 366 State Office Bldg., Providence.

SOUTH DAKOTA: *Examination.* Yankton, Dec. 6-7. *Endorsement.* Dec. 21. Sec., Dr. Gregg M. Evans, Yankton.

Nebraska June Report

Mrs. Clark Perkins, director, Bureau of Examining Boards, reports the written examination for medical licensure held at Omaha, June 12-14, 1940. The examination covered ten subjects and included 100 questions. An average of 75 per cent was required to pass. Eighty-two candidates were examined, all of whom passed. The following schools were represented:

School PASSED	Year Grad.	Number Passed
Rush Medical College	(1938)	1
Creighton Univ. School of Med.	(1938), (1939, 6), (1940, 7)	14
University of Nebraska College of Medicine	(1939), (1940, 66)	67

Nine physicians were licensed to practice medicine by reciprocity and one physician so licensed by endorsement from February 8 through July 27. The following schools were represented:

School LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Colorado School of Medicine	(1938)	Utah
The School of Medicine of the Division of Biological Sciences	(1935)	Illinois
University of Illinois College of Medicine	(1924)	Illinois
State University of Iowa College of Medicine	(1935)	Iowa
University of Michigan Medical School	(1934), (1935)	Michigan
University of Oregon Medical School	(1938)	Louisiana
Baylor University College of Medicine	(1939)	Texas
University of Western Ontario Medical School	(1936)	Michigan

School LICENSED BY ENDORSEMENT	Year Grad.	Endorsement of
Harvard Medical School	(1933)	N. B. M. Ex.

Kansas June Report

Dr. J. F. Hassig, secretary, Kansas State Board of Medical Registration and Examination, reports the written examination for medical licensure held at Kansas City, June 18-19, 1940. The examination covered ten subjects and included 100 questions. An average of 75 per cent was required to pass. Eighty candidates were examined, all of whom passed. Thirteen physicians were licensed to practice medicine by reciprocity. The following schools were represented:

School PASSED	Year Grad.	Per Cent
College of Medical Evangelists	(1940)	86
Loyola University School of Medicine	(1940)	82.9
Northwestern University Medical School	(1940)	86.5
Rush Medical College	(1939)	86
University of Kansas School of Medicine	(1940)	79.4, 82, 83.7, 84.1, 84.1, 84.3, 84.7, 84.8, 85, 85.3, 85.3, 85.4, 85.6, 86.1, 86.2, 86.2, 86.5, 86.6, 86.8, 87, 87.2, 87.3, 87.3, 87.4, 87.6, 87.6, 87.7, 88, 88.1, 88.3, 88.3, 88.5, 88.5, 88.6, 88.7, 88.7, 88.7, 88.7, 88.8, 88.8, 88.9, 89, 89.1, 89.4, 89.5, 89.5, 89.5, 89.6, 89.8, 89.8, 90.1, 90.2, 90.2, 90.5, 90.6, 90.6, 90.7, 90.7, 90.9, 91.5, 91.7, 91.9, 92, 92.4, 92.4, 92.6, 92.8, 93.5
Harvard Medical School	(1938)	86.9
Creighton University School of Medicine	(1939) (1940) 81.9, 83.2, 85.3, 86.4	85.9,
University of Pennsylvania School of Medicine	(1938)	93.8

School LICENSED BY RECIPROCITY	Year Grad.	Reciprocity with
University of Southern California School of Medicine	(1939)	California
Howard University College of Medicine	(1926)	Missouri
Loyola University School of Medicine	(1926)	Illinois
Northwestern University Medical School	(1926)	Maryland
State University of Iowa College of Medicine	(1936)	Iowa
University of Michigan Medical School	(1927)	Michigan
Medico-Chirurgical College of Kansas City	(1900)	Missouri
Creighton University School of Medicine	(1935)	New Jersey
Columbia Univ. College of Physicians and Surgeons	(1926)	S. Carolina
Vanderbilt University School of Medicine	(1936)	Mississippi
University of Texas School of Medicine	(1936)	Texas
University of Wisconsin Medical School	(1932)	N. Dakota
McGill University Faculty of Medicine	(1922)	Penna.

Book Notices

Medical Diseases of War. By Sir Arthur Hurst, M.A., D.M., F.R.C.P., Consulting Physician to Guy's Hospital, London, with the co-operation of H. W. Barber, M.A., M.B., F.R.C.P., Physician-in-Charge of the Skin Department, Guy's Hospital, F. A. Knott, M.D., M.R.C.P., Bacteriologist to Guy's Hospital, and T. A. Ross, M.D., F.R.C.P. Cloth. Price, $5.50. Pp. 327, with 38 illustrations. Baltimore: William Wood & Company, 1940.

This small volume contains much valuable and practical information. The author lays the greatest stress on functional disorders; of twenty-five chapters fifteen are devoted to functional diseases, eleven to hysteria alone. The importance of the subject may be gathered from the fact that, of 341,025 discharges from the British army, neuroses accounted for 6 per cent. The chief predisposing causes of war neuroses appeared to be the neuropathic and psychopathic inheritance and the previous nervous or mental breakdown. Such men are frequently able to lead normal lives as civilians but are totally incapable of adapting themselves to a soldier's life; in fact the author believes that these "martial misfits" should have never been enlisted. The examining boards were too exclusively concerned with the physical fitness of the recruits.

Of the many hysterical symptoms the most common were paralyses and contractures which followed trivial wounds of the limbs. Hurst insists that these could invariably be prevented by persuasion and reeducation as soon as the condition of the wound made active movement permissible. The hysterical nature of these symptoms was proved by rapid cure with psychotherapy. A temporary organic paralysis may be the starting point of the hysterical paralysis. Hysterical paraplegia may result from the perpetuation of the feeling of weakness in the legs caused by terror. There is a special chapter by T. A. Ross on psychoneuroses of war. Ross points out that the treatment of the anxiety state consists primarily in finding out what the anxiety is about. These patients with psychoneuroses were frequently full of self reproach for having feared. They feared they had been cowards. They dreaded having to go back. They feared very much that they would be sent back before they were well. Hurst and Ross are apparently in agreement as to the treatment of these symptoms. Hysterical symptoms especially could invariably be cured by simple psychotherapy in the form of explanation, persuasion and reeducation. It is pointed out, however, that a "negative reassurance" to a neurotic person does not have the slightest effect on a symptom, whereas the most elementary psychologic explanation will cause all the symptoms to disappear. There is a theoretical distinction between malingering and neurosis; namely, the malingerer is fully conscious of what he is doing and the neurotic person is not. The term "shell shock" was much abused in the last war because it was applied to almost any form of neurosis. Hurst has no objection to its use provided one has in mind a condition which has an organic basis for it consisting of the more or less evanescent changes in the nervous system resulting from the concussion caused by aerial compression. It is, however, important to remember that hysterical or anxiety symptoms are frequently superimposed on this organic basis. There is much truth in the author's statement that if it had been generally understood that shell shock was not a method of getting to England there would have been much less of it.

The chapter on soldier's heart is in essence a condensation of the views of Sir Thomas Lewis as presented in the recent edition of "The Soldier's Heart and the Effort Syndrome." The remainder of the book contains brief but informative chapters on trench fever, typhoid and paratyphoid fever, dysentery, epidemic jaundice, tetanus, war nephritis and gas poisoning. The author believes that active immunization with tetanus toxoid of all soldiers proceeding on active service will probably lead to the total disappearance of tetanus as a complication of wounds and passive immunization with antitetanic serum will no longer be necessary. A special chapter by H. W. Barber is devoted to the extremely important subject of skin diseases, in particular scabies and pediculosis. Because of its preeminently practical and authoritative grasp of the problems of military medicine, this volume cannot be too emphatically recommended as compulsory reading for the medical personnel of the examining boards and of the medical officers in active service.

La maladie de Besnier-Bœck-Schaumann: Ses manifestations cutanées, ganglionnaires, pulmonaires, osseuses, oculaires, glandulaires, viscérales, nasales, nerveuses. Par L. M. Pautrier, professeur de clinique des maladies cutanées et syphilitiques à la Faculté de médecine de Strasbourg. Paper. Price, $2.05. Pp. 341, with 105 illustrations. Paris: Masson & Cie, 1940.

The monograph by Pautrier of Strasbourg presents an interesting and authoritative discussion of the Besnier-Boeck-Schaumann disease. Part 1 deals with the evolution of the modern concept of this clinical entity. Because of its historical importance, Besnier's case of "lupus pernio" is presented in detail. This is followed by the description of sarcoid or lupoid lesions of Boeck. Pautrier himself was first to recognize uveoparotiditis of Heerfordt as one manifestation of the disease. He was likewise first to demonstrate in France a case in which there was pulmonary and lymph node involvement in the absence of cutaneous lesions. It was, however, left to Jorgen Schaumann of Stockholm to demonstrate the essential identity of these apparently unrelated clinical entities. Pautrier is emphatic in stating that it was chiefly due to the labors of Schaumann that what was once considered a rare dermatosis has become recognized as a systemic disease capable of invading any tissue or organ of the body. Part 2 is devoted to the description of the gross and microscopic lesions of the skin, mucous membranes, bones, muscles, lymphoids and blood organs, the respiratory tract, the glands, viscera, and ocular and nervous lesions. The text is profusely illustrated with excellent reproductions of photographs of the author's cases and with photomicrographs of histologic preparations.

In his discussion of the nature and the etiology of the disease the author, while acknowledging our great indebtedness to Schaumann, takes issue with him on a number of points. It appears that this new clinical entity has been rather unfortunate in acquiring a number of eponyms. Pautrier feels that the term "sarcoid" is particularly inept and certainly meaningless in cases not presenting cutaneous lesions. He admits the propriety of calling it Schaumann's disease, but to drop Besnier-Boeck would in his opinion lead to too much confusion in the literature. It is rather surprising that in his extensive discussion as to priority he does not mention Jonathan Hutchinson, whose description of a classic case of lupus pernio preceded that of Besnier by two decades. He is, however, definitely opposed to Schaumann's designation of the disease as benign lymphogranuloma. Schaumann apparently was much impressed with the regular involvement of the lymph nodes and with marked monocytosis, so that he came to consider the disease as a sort of lymphadenopathy. Pautrier's objections are based on the following arguments: 1. The disease bears little if any resemblance to other lymphogranulomas such as Hodgkin's or to venereal lymphogranuloma. 2. It displays predilection not only for the lymphatic tissue but also for the eye, the parotid gland and the hypophysis. 3. The histologic unit is not characteristic of a granuloma. In his microscopic studies the author was impressed with the fact that the histologic unit was always the same no matter where encountered. The epithelioid cells composing it are in his opinion derived from histiocytes; in other words, from reticulo-endothelial tissue. Therefore the lesion is in his opinion a reticulo-endotheliosis rather than granulomatosis. The ubiquity of the reticulo-endothelial system explains the ubiquity of the lesions of this disease. Pautrier further differs with Schaumann on the subject of etiology of the disease. Schaumann believes that it is essentially bovine tuberculosis. Pautrier objects to the tuberculosis theory on the basis of certain microscopic differences, in particular the absence of caseation, the failure to demonstrate tubercle bacilli in stained sections, cultures or animal inoculations, and negative reactivity to large doses of tuberculin. Kissmeyer's and his own statistics show that two thirds of the cases react negatively to tuberculin. Pautrier calls attention to the fact that even among the positive reactors one sees only local skin reaction but never a focal reaction. Pautrier sees a further objection to the tuberculosis theory in a certain antagonism between the two diseases, the absence of tuberculous antecedents in the history of these patients and the fact that when true tuberculous lesions develop in one of these the formerly negative reaction becomes positive, while the sarcoid lesions disappear as soon as true tuberculous lesions appear.

Salben und Salbengrundlagen: Ein Leitfaden für Ärzte und Apotheker. Von Dr. H. v. Czetsch-Lindenwald, Apotheker, Biolaboratorium Oppau der I. G. Farbenindustrie A. G., Ludwigshafen a. Rh., und Dr. F. Schmidt-La Baume, Priv.-Doz., Chefarzt der Hautabteilung der Städtischen Krankenanstalten Mannheim. Mit einem Beitrag: Die Aufgaben der Arbeitsschutzsalben. Von R. Jäger. Paper. Price, 16.80 marks. Pp. 240, with 36 illustrations. Berlin: Julius Springer, 1939.

The difficulties encountered by the authors in their effort to bring the arts of ointment prescribing and ointment making nearer the status of a science are set forth in the preface. Experiments in the laboratory were checked by trials on patients, and the utmost care was observed to make the tests accurate. The authors maintain that the question of ointment bases and their relation to absorption or diffusion of therapeutic agents presents a problem in which not only dermatologists but all physicians should interest themselves. The book is also intended to help the pharmacist, clarifying the borderland relations of pharmacognosy, pharmacology and the knowledge of colloids with pharmacy. It is offered as a bridge between the physician and the pharmacist, explaining to the latter why the physician under certain circumstances employs one ointment and in other cases needs an entirely different one.

The first chapter, after a historical review of the use of ointments, discusses the general bases of salve manufacture, fats, synthetic fats, paraffin hydrocarbons, saturated and unsaturated fatty acids, emulsions, waxes and alcohols. Next the function of ointment is considered, whether it is intended to promote resolution of the inflammation, penetration of the medicament or protection from outside influences. Ointments as carriers of various drugs, such as salicylic acid, mercury and sulfur, hormones, vitamins, bee or snake venom and many other substances are discussed and the use of local anesthetics, disinfectants and dyes in ointments is considered, with the possibility of chemical reactions taking place in the ointment. Warning is sounded against the use of pyrogallol in ointment for the production of imitation tan, which has been practiced in Germany, and the risk of kidney damage and methemoglobin formation is pointed out. The authors, in their laboratory study of the combinations of chrysarobin with various ointment bases, concluded that fats should give better results than petrolatum. Clinical trial in cases of psoriasis showed, however, that the reverse is true and they present this as an illustration of the fact that the conclusions drawn from laboratory experiments and studies of absorption may be wholly reversed by trial in the clinic. Vitamins in salves receive thorough treatment, not omitting vitamins F and H and chlorophyll, though vitamin K is not mentioned. Ointments containing cod liver oil receive attention in four pages.

The chapter on salves containing hormones is of particular interest in the light of the controversy on this question in this country. Nothing is said of the possibility of harm resulting from such ointments used as cosmetics. A striking example of the enthusiasm of European drug houses is granulomsalbe, made in Hungary, said to contain cod liver oil and extracts of testicle, skin, ovary, hypophysis cerebri and thyroid gland. According to Frenkel and Heks (*Terapia* **7**:437, 1930) the field of activity of this wonderful ointment corresponds to its complexity. The discussion ends with the remark that in most cases percutaneous hormone therapy should be used to complement the application of ointments containing hormones. Special attention is given salves for the use of the veterinarian, salves for use in the nose or eye, suppositories, the technic of production of ointments, and their testing, packing and preservation.

A pleasant relief from the serious study of ointment construction and use is the short consideration of ancient types of ointment still in circulation, such as those used for witchcraft. The authors quote a Swiss journal's description of an ointment to be applied to the axillas and about the genitalia which is guaranteed to produce pleasant dreams. In the analysis traces of alkaloids were found, which explains the recommendation that the salve be applied to parts secreting alkaline sweat. Evidently the producers later became cautious and reduced the amount of active ingredients to protect themselves. The American cosmetic industry comes in for attention. Navaree is quoted on the constituents of an "eyelash food." Yellow petrolatum perfumed with ethereal oils is completed by the addition of turtle oil. The latter is necessary, no doubt, is the comment, because of its content of valuable hormones, those that are responsible for the great length of the eyelashes of the tortoise.

The book ends with a plea for more attention to salve bases and salve construction in the daily work of the physician and pharmacist, if they are not intent on being outstripped in this matter by the maker of cosmetics. A simple list of five types of ointment bases is given, from which the physician can choose, depending on the effect desired. An excellent summary sets forth briefly the indications for the various salve types. Apologizing for the fact that not all known ointments have been mentioned, the authors explain that their aim has been to describe types and to mention the most important examples of each type, to avoid complexity.

The appendix, a discussion by R. Jäger of the structure and function of salves intended to protect workmen against irritating substances in industry, is a valuable and practical treatise. The author, while not able to offer any short and sure method of protection against all the cutaneous hazards of industry, suggests a scientific and practical method of attacking the problems as they arise.

The book is a mine of useful information for the physician, the pharmacist and the maker of cosmetics.

Manual of Peripheral Vascular Disorders. By David W. Kramer, M.D., F.A.C.P., Assistant Professor of Medicine, Jefferson Medical College, Philadelphia. Cloth. Price, $6. Pp. 448, with 126 illustrations. Philadelphia: Blakiston Company, 1940.

The general plan of this book is excellent. There are chapters on symptoms, history taking, physical examination, methods of studying circulation, evaluation of various tests of circulatory function, clinical application of circulatory tests, occlusive vascular disorders of various forms, treatment, vasospastic and vasodilator disorders, hypertension, traumatic vasospasm, gangrene and disorders of veins. Lymphedema is not considered.

While many phases of the subjects presented are admittedly controversial, many statements are made which conflict with the views of accepted experts in the field of peripheral circulation. These statements should not detract greatly from the value of the book. The author writes that claudication is "frequently" relieved by rest. It always is. He states that circulation is normal if pulsations in the dorsalis pedis and posterior tibial arteries are normal, yet there have been reports of thromboangiitis obliterans involving digital arteries when pulsations were normal in the dorsalis pedis and posterior tibial arteries. The statement is made that Negroes do not have thromboangiitis obliterans. That is an opinion contrary to at least one excellent report. Contrary to the author's opinion, bruits are frequently absent in congenital arteriovenous fistula. Also decompensation of the heart is relatively rare when acquired arteriovenous fistula is first recognized. The author implies that cardiac decompensation is always present. He does not support his contention that diabetic "arteritis" is a form of inflammatory occlusive arterial disease; he is inconsistent in classifying "chronic arteritis" under noninflammatory occlusive vascular disorders; he gives no reason for designating arteriovenous fistula as a form of occlusive arterial disease (which it isn't); he confuses temporal arteritis with periarteritis nodosa and he fails to give evidence as to why neurotropic disorders, such as syringomyelia, should be considered occlusive vascular disorders. The statement that thrombo-angiitis obliterans never has an acute onset neglects reports in the medical literature. It is improbable that "endarteritis obliterans," as described by the author, is a clinical or pathologic entity. Few will agree that peripheral endarteritis is caused by syphilis, and the author has proved only that patients with chronic occlusive arterial diseases occasionally have syphilis. Nothing is said of the desirability of using heparin in arterial embolism. Contrary to the author's statement, erythromelalgia is not always bilateral. The quotation of a classification of essential hypertension lacks accuracy. There is so little in the seven pages on hypertension that they might well have been omitted. There is emphasis on the value of the reaction of the skin to intracutaneous injection of histamine, a test which the author has used extensively, but in many clinics this procedure has been found unnecessary.

Some of the presentation lacks clearness and conciseness and in some parts even the experienced physician may become con-

fused. It is apparent that the subject of peripheral vascular diseases has become too complex for mastery by one person.

The monograph has many virtues. That the author has not supported some particular type of treatment to the virtual exclusion of others, as authors of various monographs on this subject have done, is refreshing. Treatment is emphasized. The chapters which consider methods of studying circulation are generally good. The custom of presenting important points in differential diagnosis in tabular form is desirable. The bibliography seems reasonably complete. This is certainly one of the better monographs on peripheral vascular diseases and is a distinct contribution to the rapidly growing literature on this subject.

Pneumonia and Its Nursing Care. By Herbert K. Ensworth, M.D., Instructor in Medicine, Cornell University Medical College, New York, and Lela L. Greenwood, B.A., R.N., Supervisor of Medical Pavilion, Bellevue Hospital, New York. With a foreword by Russell L. Cecil, M.D. Cloth. Price, $1.50. Pp. 177, with 44 illustrations. Philadelphia, Montreal & London: J. B. Lippincott Company, 1940.

This booklet contains an account of pneumonia and its modern treatment such as every nurse and intelligent layman should possess. The sections devoted to nursing care are amateurish, and considerable supplementary information would be required by a nurse in the field. It is profusely but not well illustrated, many of the halftones having little instructional value in a nurses' manual. The apparatus is poorly chosen; a single stage regulator is shown. The statement "an oxygen cylinder would last six or seven hours" without reference to the liter flow rate is not helpful. The technic of a nurse collecting sputum with the tent opened shows, unless the motor has been stopped, a wasteful loss of oxygen-enriched air. It is preferable to pass the arm under the skirt of the tent. A thermometer and hygrometer should be in every tent, but the authors neither picture nor refer to them. The principles of tent operation are inadequately discussed, and instructions for measuring the oxygen concentration in the tent are not given. The need for protecting the open box oxygen tent from strong currents of air is not mentioned. A disproportionate amount of space and illustration is devoted to the closed puncture drainage operation for empyema. In most cases of pneumococcic pneumonia this type of operation is inapplicable because there is an abundant pleural deposit of fibrin. The section on diet might have been advantageously expanded. The great importance of adequate salt intake is insufficiently stressed. The advances in practice which will probably come in this rapidly changing field may require another edition, at which time deficiencies, especially in the nursing sections, may be corrected.

Electrocardiography. By Chauncey C. Maher, B.S., M.D., Assistant Professor of Medicine, Northwestern University and the Montgomery Ward Medical Clinics, Chicago, and Paul H. Wosika, M.D., M.S., Instructor in Medicine, Northwestern University and the Montgomery Ward Medical Clinics. Third edition. Cloth. Price, $4. Pp. 334, with 147 illustrations. Baltimore: William Wood & Company, 1940.

The purpose of this book is to furnish physicians and students not fully trained in cardiology with an introduction to the electrocardiographic method. In presenting the third edition the authors have included consideration of the fourth lead, have utilized the standard nomenclature advocated by the American Heart Association and have correlated their terminology with the usage of everyday practice. Delineation of the basic principles underlying electrocardiography and a concise statement of the clinical aspects of the arrhythmias precede the electrocardiographic portrayal of the various disorders of the heart beat. Succeeding chapters include descriptions of ventricular conduction defects, the changes caused by coronary arterial disease, the effects of drugs, and a summary of the electrocardiographic abnormalities associated with different clinical syndromes. The volume is profusely illustrated by well selected electrocardiograms. Forty-two figures diagrammatically illustrate the physiologic and pathologic aspects of the subject and include additional electrocardiographic examples. Throughout the text the close interrelationship between the clinical aspects of heart disease and the electrocardiographic results is stressed. The authors are to be commended for their repeated caution that "the electrocardiogram is only a part of cardiac diagnostic examination. The history, the objective physical findings, the x-ray, fluoroscopy and laboratory tests all contribute positive or negative information. . . . Overemphasis of the diagnostic significance of minor defects of the QRS and T waves in an electrocardiogram with other findings normal may lead to unwarranted invalidism. . . . The interpretation of this technical data into clinical evidence is a matter of judicious consideration." The volume is essentially a practical manual for clinicians and as such can be warmly recommended to those who wish to orient themselves in this field.

Diseases of the Digestive System and Food Allergy. By Josef S. Smul, M.D., Assoc. Gastro-Ent., Beth David Hospital, New York. Cloth. Price, $3.50. Pp. 219. New York: Medical Library Company, 1940.

This curious book was written by a man who seems to have the idea that most diseases of the digestive tract, including cancer of the stomach and amebic dysentery, should be treated with a diet consisting of what he calls anallergic foods. Most curiously he includes among these anallergic foods such items as milk, eggs, wheat, cocoa, tomatoes and melons, which, according to all allergists, are looked on as the worst of offenders. The author believes that what he calls alimentallergy can now replace more than fifty clinical syndromes previously recognized under other names. As one would expect, he furnishes no adequate proof for his astounding doctrines. We suspect the book will be of interest only to collectors of medical curios.

The Diagnosis and Treatment of Diseases of the Peripheral Arteries. By Saul S. Samuels, A.M., M.D., Chief of the Clinic for Peripheral Arterial Diseases, Fourth Division, Bellevue Hospital, New York. Second edition. Cloth. Price, $6.50. Pp. 372, with 106 illustrations. New York, Toronto & London: Oxford University Press, 1940.

In the present edition this monograph has been greatly enlarged. New chapters have been added on acrocyanosis, periarteritis nodosa, embolism, cervical rib and scalenus syndrome, axillary vein thrombosis, frost bite, glomus tumor and aneurysm of the peripheral vessels. The number of illustrations has been increased. Thus the book has really become a much more rounded out discussion of peripheral circulatory disturbances; because of their frequency, thrombo-angiitis obliterans and arteriosclerosis obliterans have received most of the space. The clear lucid style of the author makes for pleasant and instructive reading. His experience in this field is obvious. The diagnostic methods are simple and his logic of treatment is sound and safe. Great emphasis is laid on oscillometric readings and on the value of color changes; little value is ascribed to the venous filling time and to the histamine and salt wheals. In the treatment of peripheral vascular disorders the author does not advocate suction and pressure therapy, intermittent venous hyperemia, typhoid vaccine injections, whirlpool baths and contrast baths. Hot sitz baths, diathermy and hypertonic salt solutions are favored. The vasomotor component in organic vascular disease does not play an important part in the author's opinion. Sympathetic ganglionectomy and crushing of peripheral nerves are not indicated in the organic vascular disorders. Even in Raynaud's disease, sympathectomy occupies a small place in the author's methods of treatment. This monograph is an excellent account of the author's methods of diagnosis and therapy. As such it is interesting and instructive reading for those who are especially interested in this field. While the subject material has been greatly extended compared with the first edition, it still lacks a wider concept of peripheral vascular disease and hardly covers the achievements of other workers. The general practitioner will not find it a review of the latest developments.

La costituzione della donna e la lotta contro i fattori di sterilità. Atti della 1ª settimana medica internazionale di Salsomaggiore (29 agosto -4 setembre 1937—A. XV). Publicati dalle RR. Terme a cura del Prof. V. de Blasi, docente di Clinica ostetrico-ginecologica nella R. Università di Genova. Paper. Price, 65 lire. Pp. 788, with illustrations. Rome: Luigi Pozzi, 1938.

This work is a compilation of articles presented by various European gynecologists at the international medical convention at Salsomaggiore, Italy, in September 1937. It discusses the subject from an etiologic and therapeutic standpoint. These meetings were encouraged by the Fascist government, whose Duce believes "that strong and fertile human beings are more important for a nation than bars of gold in the treasury." A special emphasis is made of the importance in maintaining a balanced psychoneuro-endocrine system to avoid genital insuf-

ficiency. Throughout the work emphasis is likewise placed on the therapeutic value of the Salsomaggiore waters in augmenting endocrine treatment. A classification of the various waters, the different modes of applying this treatment and the rationale of their action are stressed. In a discussion of sports on the maternal function, the author concludes that moderate and sensibly practiced sports increase rather than impair woman's fecundity. The articles add little to the subject of sterility. Considerable repetition as well as a noticeable lack of data and illustrations are apparent.

Les jours de l'homme. Par le Docteur Besançon. Paper. Price, 15 francs. Pp. 149. Paris: Vigot Frères, 1939.

In this essay on longevity the author, an octogenarian, discusses the problem from various angles and comes to some startling conclusions. Four factors are responsible for longevity: (1) continuous flow of sex hormones, (2) mental activity, (3) transmitted diseases and (4) heredity. Mental activity, he says, is necessary for rejuvenation of the brain cells. Many priests, physicians, writers and other intellectuals live long, and more men than women reach old age because brain work required by their profession renovates their hormones. As to the third factor, two thirds of the entire medical field is covered by two groups of diseases: (1) diseases of species, chiefly of an infectious origin, and (2) diseases of individuals, mostly of a nervous character, transmitted from the father to his descendants and represented by a long array of such conditions as eczema, asthma, migraine, dyspepsia, nervous diarrhea, hemorrhoids, lithiasis and diabetes. If such functional diseases persist, longevity may be expected because the patient pays in small instalments his debt for the privilege of living long. It follows that such ailments should not be suppressed, because if they are exterminated the patient may share the fate of his disease. The essay ends with a eulogy of physicians. Malgaigne used to give the following advice: "If your son is intelligent, make an internist out of him; if he is stupid let him be an obstetrician, and if he has no brains but has a manual skill, train him in surgery." Most of the authors' conclusions and remarks do not require comment; they resemble an issue of Tonics and Sedatives.

Tomography. By J. B. McDougall, M.D., F.R.C.P., F.R.S.E., Medical Director, Preston Hall, Maidstone, Kent. Cloth. Price, 21s. Pp. 73, with 110 illustrations. London: H. K. Lewis & Co., Ltd., 1940.

The author has attempted to demonstrate the value of tomography in the diagnosis of pulmonary tuberculosis. Those not familiar with the term will appreciate the explanation that tomography is intended to indicate sectional radiography. It has otherwise been described as planigraphy, stratigraphy and laminagraphy. One author has referred to the instrument for making tomograms as an "x-ray focusing machine." In other words, it is a method whereby the parts to be examined may be studied at previously determined depths. The author argues that tomography is superior to the stereoscopic method. Numerous illustrations illuminate the work, which is in atlas form. The author is not very convincing in his attempt to minimize the value of the stereoscopic method in pulmonary tuberculosis. In certain cases tomography seems to have definite superior value.

Diesel Engines Underground. I: Composition of Exhaust Gas from Engines in Proper Mechanical Condition. By John C. Holtz, L. B. Berger, M. A. Elliott and H. H. Schrenk. United States Department of the Interior, Bureau of Mines. Report of Investigations 3508. Paper. Pp. 48. Pittsburgh, 1940.

The use of internal combustion engines in underground mining operations presents several interesting problems involving safety and health. This study deals with the nature of the exhaust gases from Diesel motors. These gases may be hot enough to ignite inflammable atmospheres in mines and contain definitely toxic constituents. Variations in use result in changes in the nature of the exhaust gases, but even under optimum conditions of speed, power output and fuel-air ratio, sufficient quantities of carbon monoxide, carbon dioxide, the oxides of nitrogen and aldehydes are produced to make ventilation necessary.

Les pneumolyses chirurgicales dans le traitement de la tuberculose pulmonaire. Par Jean Chenebault. Paper. Pp. 473, with 42 illustrations. Paris: Libraire Louis Arnette, 1939.

The title might be freely translated to read My Experiences with Extrapleural Pneumothorax, a Review of Over 150 Cases. If this were the title it would tell exactly what the book is about. Chenebault prefers the term pneumolyses to extrapleural pneumothorax and further distinguishes between two types: the parapneumolyses, which correspond to what we call extrapleural pneumothorax, and telepneumolyses, which correspond to the procedure employed in doing an apicolyses according to Semb. The entire subject is discussed: the history, through anatomy, pathologic anatomy and technic. The last part of the book deals with a report of 115 cases of extrapleural pneumothorax, twenty-one cases of extrapleural pneumothorax associated with thoracoplasty and thirty-seven cases of "telepneumolyses" associated with thoracoplasty. The book is written in French. It is well written and readable. The final chapter sums up the author's opinion on the entire subject. There is a good bibliography. The book should be on the shelf of any one making a study of the collapse treatment of tuberculosis.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Fraudulent Concealment as Tolling Running of the Statute of Limitations.—The plaintiff brought suit for malpractice against the three physician defendants in December 1935. He alleged, essentially, that (1) in operating on his wife in 1930 they left two sponges in her abdomen, (2) they allowed her to leave the hospital about fifteen days after the operation while she still had an elevated temperature, without informing her or him of the presence of the sponges and without giving any instruction as to further treatment, and (3) the patient suffered continuously thereafter, necessitating another operation in June 1935, when sponges were discovered in her abdomen and were removed. The plaintiff filed three different amended petitions, the last one in 1938. In the last amended petition he alleged for the first time that the physicians during the operation in 1930 and at all times thereafter knew of the presence of the sponges in the patient's abdomen and fraudulently concealed from him and from the patient their presence and the necessity for removing them. Each physician, in separate answers, took exception to the third amended petition on the ground that it was barred by the applicable two year statute of limitations. They claimed that the plaintiff's cause of action based on malpractice had accrued more than two years before the commencement of the suit and that the cause of action based on the alleged fraud of the defendants had likewise accrued more than two years prior to the first filing of any allegations charging fraud. The court sustained the exceptions and dismissed the suit, and the plaintiff appealed to the court of civil appeals of Texas, Waco.

The plaintiff contended that the action of the trial court was in error, arguing that (1) the two year statute of limitations could not be regarded as running against him until such time as he could reasonably be charged with knowledge that the sponges had been left in his wife's abdominal cavity; (2) the physicians' failure to inform him or his wife of the presence of the sponges in the latter's body tolled the statute of limitations until such time as the presence of the sponges was discovered or should have been discovered, and (3) the charge of fraudulent concealment, contained for the first time in his third amended petition, did not constitute a new and independent cause of action. But, said the court of civil appeals, by the apparent weight of authority a physician's failure to remove a sponge before closing an incision is negligence as a matter of law. Generally the statute of limitations commences to run in such a case as the instant one from the time the duty owing to the plaintiff is breached by the wrongful or negligent act of the defendant, even though the plaintiff is ignorant of the existence of the cause

of action or even though damages are not sustained until after the commission of the tort. But if, as the plaintiff alleged, the defendants in this case knew at the time and continuously after the incision was closed that sponges had been negligently left in the patient's abdomen, and if they discharged her without disclosing the situation and without suggestion or advice as to further treatment, the statute would have been tolled until the fraud was, or could by the exercise of reasonable diligence have been, discovered. Consequently, the trial court should have heard evidence to enable it to determine whether or not there had been a fraudulent concealment, as was alleged by the plaintiff. While the fraudulent concealment of a cause of action by a defendant will prevent the bar of the statute of limitation if the plaintiff in the exercise of ordinary diligence fails to discover the existence of a cause of action, fraudulent concealment of a cause of action is not in itself a cause of action separate and apart from the underlying malpractice. The fraudulent concealment merely estops the guilty party from asserting or relying on the defense of limitations until his fraud is, or by the exercise of ordinary diligence could have been, discovered by the plaintiff. If, continued the court, such a situation existed in the instant case, the plaintiff's cause of action may have appeared to be barred at the time he filed his suit, but it was not in fact barred if the defendant physicians were estopped to rely on the defense of limitation because they had fraudulently concealed the cause of action. Whether it was barred in fact will depend on the testimony which may be presented at a future trial.

For the reasons above stated, the court concluded that the trial court had erred in sustaining the exceptions, and accordingly it reversed the judgment of dismissal and remanded the cause for a new trial.—*Thompson v. Barnard (Texas), 142 S. W. (2d) 238.*

Malpractice: Liability for Injury to Patient from Nurse's Operation of Fluoroscope.—The plaintiff was referred by her attending physician to the defendant physicians for fluoroscopic examinations. The fluoroscope owned by the defendants was one manufactured by the defendant Black Company. On Jan. 19, 1937, the plaintiff, as she had done preparatory to examination on six prior occasions, stepped up on the foot rest of the fluoroscope and placed her back against the fluoroscopic table which was in a perpendicular position. A nurse employed by one of the defendant physicians, by means of a switch, turned on the electric current which was supposed to cause a system of gears to tilt the table backward so that the plaintiff would lie on it in a horizontal position. While the apparatus was being so operated a pin in the gear system broke because of crystallization and, although the defendant nurse turned the switch in the opposite direction in an attempt to reverse the movement of the apparatus, the table continued to move backward rapidly beyond the horizontal position. The plaintiff was thrown backward off the table, striking her neck and shoulders against the wall and floor. She sustained injuries, to recover damages for which she brought suit against the defendants, the two physicians, the nurse and the manufacturer. From a judgment of the trial court in favor of the defendants, the plaintiff appealed to the district court of appeal, first district, division 2, California.

The plaintiff based her case on the theory that the doctrine of res ipsa loquitur was applicable. She contended that, since she had shown that the fluoroscopic apparatus which had caused her injuries was under the management of the defendants and that the accident was one which would not have happened ordinarily if those who managed the use of the apparatus had exercised proper care, an inference arose, in the absence of an explanation by the defendants, that the accident had been caused from their lack of proper care. The district court of appeals, however, was of the opinion that, assuming that the doctrine of res ipsa loquitur was applicable, the plaintiff had adduced no evidence which would have supported a verdict in her favor. The court could not agree with her contention that the defendant nurse was incompetent to operate the fluoroscopic apparatus. The nurse's undisputed testimony showed that she was competent and that she had had several years of experience in operating a fluoroscope. With respect to the plaintiff's claim that the nurse had no license to operate a fluoroscope the court pointed out that she had failed to indicate what license a person needs to operate a fluoroscopic table, a barber chair or any other tilting chair. In operating the switch the nurse committed no act of negligence because, as the evidence disclosed, after the pin broke the table was out of control and its motion was unaffected by any movement of the switch. In the judgment of the court, the plaintiff had failed to prove that the defendants were negligent.

Also, continued the court, assuming that the doctrine of res ipsa loquitur was applicable, any possible presumption in favor of the plaintiff was rebutted by evidence introduced by the defendants. They showed that the fluoroscope used had been purchased from a reliable manufacturer only eight years prior to the date of the accident; that the apparatus was of standard make; that many such machines were in use in California and elsewhere and had been used for as long as twenty-five years, and that the fluoroscopic table in question had been used daily and at frequent intervals had been oiled, inspected and repaired. The defendant physicians, said the court, were required to exercise only reasonable care to protect the plaintiff, an invitee, from injury by making ordinary examinations of their equipment. In making a proper examination the defendants were not required, as the plaintiff contended, to go to such lengths as to cause the gear box of the apparatus to be taken off from time to time, the gears removed and the pin taken out of its socket and subjected to the roentgen ray to detect any possible crystallization. Prior to the moment of the accident, the defendants had no notice of any defect in their apparatus because nothing had occurred to indicate that the pin had become weakened or worn. In the judgment of the court, latent defects which are either concealed in defective workmanship or are incidental to ordinary wear and tear of usage are among those casualties which no man can avoid without the exercise of that extraordinary care and vigilance which the law does not impose.

Accordingly, the district court of appeal affirmed the judgment in favor of the defendants.—*Johnston v. Black Co. et al. (Calif.), 91 P. (2d) 921.*

Society Proceedings

COMING MEETINGS

American Academy of Ophthalmology and Oto-Laryngology, Cleveland, Oct. 6-10. Dr. William P. Wherry, 107 South 17th St., Omaha, Secretary.

American Academy of Pediatrics, Memphis, Tenn., Nov. 18-20. Dr. Clifford G. Grulee, 636 Church Street, Evanston, Ill., Secretary.

American Clinical and Climatological Association, White Sulphur Springs, W. Va., Oct. 28-30. Dr. Francis M. Rackemann, 263 Beacon St., Boston, Secretary.

American College of Surgeons, Chicago, Oct. 21-25. Dr. Frederic A. Besley, 40 East Erie St., Chicago, Secretary.

American Public Health Association, Detroit, Oct. 8-11. Dr. Reginald M. Atwater, 50 West 50th St., New York, Executive Secretary.

American Roentgen Ray Society, Boston, Oct. 1-4. Dr. Carleton B. Peirce, Royal Victoria Hospital, Montreal, Canada, Secretary.

American Society of Anesthetists, New York, Oct. 10. Dr. Paul M. Wood, 745 Fifth Avenue, New York, Secretary.

American Society of Tropical Medicine, Louisville, Ky., Nov. 12-15. Dr. E. Harold Hinman, Malaria Control Division, Wilson Dam, Ala., Secretary.

Association of Military Surgeons of the United States, Cleveland, Oct. 10-12. Dr. H. L. Gilchrist, Army Medical Museum, Washington, D. C., Secretary.

Central Society for Clinical Research, Chicago, Nov. 1-2. Dr. Carl V. Moore, Washington University School of Medicine, St. Louis, Secretary.

Clinical Orthopaedic Society, Milwaukee and Madison, Wis., Oct. 18-19. Dr. Myron O. Henry, 825 Nicollet Ave., Minneapolis, Secretary.

District of Columbia, Medical Society of the, Washington, Oct. 15-17. Mr. Theodore Wiprud, 1718 M St., N.W., Washington, Secretary.

Indiana State Medical Association, French Lick, Oct. 29-31. Mr. Thomas A. Hendricks, 23 East Ohio St., Indianapolis, Executive Secretary.

Inter-State Postgraduate Medical Association of North America, Cleveland, Oct. 14-18. Dr. W. B. Peck, 27 East Stephenson St., Freeport, Ill., Managing Director.

Nevada State Medical Association, Las Vegas, Oct. 11-12. Dr. Horace J. Brown, 120 North Virginia St., Reno, Secretary.

New York State Association of Public Health Laboratories, Albany, Nov. 1. Miss Mary B. Kirkbride, New Scotland Avenue, Albany, Secretary.

Omaha Mid-West Clinical Society, Omaha, Oct. 28-Nov. 1. Dr. J. D. McCarthy, 107 South 17th St., Omaha, Secretary.

Pacific Coast Society of Obstetrics and Gynecology, San Francisco, Nov. 6-9. Dr. T. Floyd Bell, 400 Twenty-Ninth St., Oakland, Calif., Secretary.

Pennsylvania, Medical Society of the State of, Philadelphia, Sept. 30-Oct. 3. Dr. Walter F. Donaldson, 500 Penn Ave., Pittsburgh, Secretary.

Southern Medical Association, Louisville, Ky., Nov. 12-15. Mr. C. P. Loranz, Empire Bldg., Birmingham, Ala., Secretary.

Southwestern Medical Association, Tucson, Ariz., Nov. 21-23. Dr. M. P. Spearman, 1001 First National Bank Bldg., El Paso, Texas, Secretary.

Vermont State Medical Society, Rutland, Oct. 9-10. Dr. B. F. Cook, 154 Bellevue Ave., Rutland, Secretary.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1930 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

American Journal of Cancer, New York

39:309-462 (July) 1940

Experimental Studies on Relation of Pregnancy to Leukemia. J. H. Burchenal, New York.—p. 309.
Increase in Incidence of Lymphomatosis in Male Fowls by Castration. D. Marine and S. H. Rosen, New York.—p. 315.
Direct and Indirect Effects of Roentgen Radiation on Blood Forming Organs of Rats. C. L. Hsü and W. C. Ma, Peiping, China.—p. 319.
Spontaneous Primary Carcinoma of Prostate in Monkey (Macaca Mulatta). E. T. Engle and A. P. Stout, New York.—p. 334.
Effect of Fat on Tumor Formation. H. P. Jacobi and C. A. Baumann, Madison, Wis.—p. 338.
Rhabdomyosarcomatous Pulmonary Metastases from Teratoma Testis. M. D. Bosse, Pittsburgh.—p. 343.
Genetic Analysis of Induction of Tumors by Methylcholanthrene: Note on Origin of NH Strain of Mice. L. C. Strong, New Haven, Conn. —p. 347.
Effect of Hormones on Cells Grown in Vitro: I. Effect of Sex Hormones on Fibroblasts. E. Von Haam and L. Cappel, Columbus, Ohio. —p. 350.
Id.: II. Effect of Hormones from Thyroid, Pancreas and Adrenal Gland. E. Von Haam and L. Cappel, Columbus, Ohio.—p. 354.
Specific Precipitin Antiserum for Carcinoma Protein. L. S. Mann and W. H. Welker, Chicago.—p. 360.
Further Experim ts on Effect of Carcinogenic Hydrocarbons on Elimination of Congo Red from Circulation. Cornelia Hoch-Ligeti, London, England.—p. 365.
Carcinogenic Properties of Ortho-Amidoazotoluol. H. C. Vassiliadis, Athens, Greece.—p. 377.
Fraction of Human Urine Causing Fetus Resorption in Rats and Mice. J. O. Ely, Philadelphia.—p. 379.
Chemical Compounds as Carcinogenic Agents: Second Supplementary Report: Literature of 1938 and 1939. J. W. Cook, London, England, and E. L. Kennaway, Glasgow, Scotland.—p. 381.

American J. Digestive Diseases, Huntington, Ind.

7:323-364 (Aug.) 1940

Analysis of 256 Gastroscopies Performed at Bellevue Hospital. J. Flexner and A. Fleishman, New York.—p. 323.
*Management of Acute Cholecystitis. J. E. Berk, Philadelphia.—p. 325.
Color Photography Through the Sigmoidoscope. Z. Bercovitz and C. C. Fuller, New York.—p. 332.
Effect of Various Bile Acids on Volume and Certain Constituents of Bile. A. L. Berman, E. Snapp, A. C. Ivy, A. J. Atkinson and V. S. Hough, Chicago.—p. 333.
Notes on Some Recent Books on Psychoneuroses and Minor Psychopathies. W. C. Alvarez, Rochester, Minn.—p. 346.

Management of Acute Cholecystitis.—Berk presents arguments advanced by the group who regard acute cholecystitis as an immediate surgical emergency and the group who contend that operation should be delayed until the acute stage has subsided. He concludes that: 1. Acute cholecystitis is usually dependent on an obstruction to the outlet of the gallbladder with interruption in the blood supply to the organ. In more than 92 per cent of cases the obstructing agent is a calculus. Secondary infection of the ischemic areas may be present. 2. Acute cholecystitis is a dangerous condition. Under conservative treatment about 25 per cent of the patients will get worse. Complications such as empyema, gangrene, perforation of the gallbladder and generalized peritonitis occur frequently. 3. There is no dependable correlation between the severity of the clinical manifestations and the severity of the disease. It is impossible to predict the outcome. 4. Statistics show that the mortality is great among the "early" operations done after the symptoms have been present for forty-eight hours. Operations done within forty-eight hours have had the lowest mortality rate. Unfortunately few patients reach a hospital within this interval. 5. It is inadvisable to operate on every patient seen within this time as many diagnoses will be wrong. 6. Patients and the disease vary widely and the treatment must be individualized. 7. A plan of procedure which has been employed successfully in the management of patients is as follows: immediate hospitalization and immediate operation when perforation and peritonitis are present and conservative treatment, if the condition permits, for twenty-four or thirty-six hours followed by operation if the general condition does not improve; a conservative attitude is maintained if improvement is noted.

American Journal of Medical Sciences, Philadelphia

200:145-288 (Aug.) 1940

*Pernicious Anemia: Erythrocyte Response to Treatment. M. C. Riddle, Portland, Ore.—p. 145.
Blood of Newborn Rats After Oral Administration to Mother of Normal and Abnormal Human Gastric Juice. C. P. Schlicke, Rochester, Minn. —p. 155.
Hemolysinic Anemia and Hepatic Degeneration Cured by Splenectomy. G. E. Farrar Jr., W. E. Burnett and A. J. Steigman, Philadelphia. —p. 164.
Erythrocyte Morphology in Experimental Hemolytic Anemia as Induced by Specific Hemolysin. W. D. Tigertt and C. N. Duncan, with technical assistance of A. J. Hight, Dallas, Texas.—p. 173.
Effects of Sulfanilamide and Sulfapyridine on Blood Pigments of White Rats. P. K. Smith, New Haven, Conn.—p. 183.
Coronary Embolism: Complication of Syphilitic Aortitis: Report of Three Cases. W. B. Porter and E. W. Vaughan, Richmond, Va. —p. 184.
Dissecting Aneurysm of Aorta with Experimental Atherosclerosis. S. Weiss, Boston; T. D. Kinney and Mary M. Maher, New Haven, Conn. —p. 192.
*Complete Occlusion of Abdominal Aorta: Review of Seven Cases. H. Gross and B. Philips, New York.—p. 203.
Value of Ether Circulation Time in Diagnosis of Right Heart Failure. S. Baer and H. J. Isard, Philadelphia.—p. 209.
Human Sternal Bone Marrow in Hyperthyroid and Myxedematous States. R. M. Jones, Chicago.—p. 211.
Quantitative Study of Height of Thyroid Acinar Cells in Normal and Abnormal Thyroids. M. S. Abel, Philadelphia.—p. 220.
Influence of Estrogen on Insulin Requirement of the Diabetic. Anna R. Spiegelman, New York.—p. 228.
Calcium and Phosphorus in Cerebrospinal Fluid in Diabetes Insipidus. H. Blotner, Boston.—p. 235.
Maintenance of Nitrogen Equilibrium of Amino Acids Administered Parenterally. S. S. Altshuler, Detroit; Hilda M. Hensel, Eloise, Mich., and M. Sahyun, Detroit.—p. 239.
Vitamin C Nutrition in Pellagra. Grace A. Goldsmith, A. T. Ogaard, New Orleans, and D. F. Gowe, Ponce, Puerto Rico.—p. 244.
Comparative Study of Boerner-Lukens Complement Fixation Test. R. A. Kilduffe and Doris B. Davis, Atlantic City, N. J.—p. 249.
Acute Lymphocytic Choriomeningitis: Report of Three Cases with Histopathologic Findings. W. L. Silcott and K. Neubuerger, Denver. —p. 253.
Certain Factors Governing Incidence of Cerebrovascular Crises. D. L. Dozzi, Philadelphia.—p. 259.
Effect of Partial Hepatectomy on Action of Certain Barbiturates and Phenylurea Derivative. C. H. Scheifley and G. M. Higgins, Rochester, Minn.—p. 264.

Pernicious Anemia: Erythrocyte Response to Treatment.—Riddle points out that Minot and his associates, soon after their discovery of the therapeutic effectiveness of liver in pernicious anemia, recognized certain quantitative relationships between the erythrocyte count before treatment, the dose of liver employed in treatment, the number of reticulocytes which appeared early in remission, and the increase in the erythrocyte count. They were impressed particularly by the importance of the large number of reticulocytes in the blood in the first phase of the remission following liver therapy, and they and others devised mathematical equations which represent the numbers or percentage of reticulocytes which may be expected to appear in individual patients with pernicious anemia adequately treated. Although these standard reticulocyte equations have proved useful their value has been disputed, particularly by Murphy. Riddle cites Murphy to the effect that rise in the erythrocyte count would be a far simpler method of evaluating the treatment than the reticulocyte response, if the expected erythrocyte increase were expressed in as simple and as accurate form as the standard reticulocyte equations. The author studied a large number of remissions to determine the quantitative relationships between the rate of erythrocyte increase and the erythrocyte count before treatment. From data of 523 patients with pernicious anemia satisfactorily treated, the average weekly increase in the erythrocyte count at the end of two weeks of treatment was found to bear an inverse relationship to the erythrocyte count before treatment. This relationship is expressed in the equation $I = 0.78 - 0.174Eo$, where I is the average weekly increase in the erythrocyte count after two weeks of treatment and Eo the

erythrocyte count before treatment expressed as millions of erythrocytes per cubic millimeter of blood. This equation is suggested as a standard for measuring the relative effectiveness of treatment in pernicious anemia. Observed values equal to or greater than those obtained from this equation indicate adequate treatment. Observed values less than those calculated from the equation indicate inadequate treatment. The existence of various complicating factors such as concurrent disease, transfusion or hemorrhage in association with pernicious anemia invalidate the use of this standard.

Complete Occlusion of Abdominal Aorta.—According to Gross and Philips, complete occlusion of the aorta at its bifurcation has been associated clinically with a well delineated group of symptoms. The classic syndrome is one of acute onset with severe pain and loss of sensation in the legs, absence of arterial pulsations and rapidly progressive ascending gangrene of the lower extremities with fatal outcome. In a study of the clinical course of patients in whom, at postmortem, complete obstruction of the aorta was found at its bifurcation, the authors have found that this clinical picture is not constant. They present seven cases of complete occlusion of the aorta at its bifurcation, observed among 5,350 necropsies. Of these, four were patients with atherosclerosis of the coronary arteries and aorta, two with diffuse vascular disease involving the venous system and one with chronic rheumatic cardiovalvular disease, auricular fibrillation and a ball-valve thrombus of the left auricle. The classic clinical picture usually associated with complete occlusion of the aorta at its bifurcation occurred in only one of the first group of four. In another of this group there was nothing in the clinical course to suggest involvement of the aorta but at postmortem the bifurcation was completely occluded by an old gray thrombus. Of interest in the other two is the rapid progress of gangrene with speedy involvement of the opposite extremity. In the two cases with diffuse vascular disease, the aortic involvement seemed to be a mere incident in the course of a progressive disease involving the entire arterial tree with an arteritis in one and venous involvement in the other. The last case resembles in almost every detail the cases described in the literature in which complete occlusion at the bifurcation of the aorta occurred as a complication of chronic rheumatic heart disease with arrhythmia and intracardiac thrombi. The differentiation of embolism from thrombosis as a cause of occlusion of the aorta is difficult. Welch thought that a decision as to the existence of one or the other is often guesswork. Neuhof pointed out that the mode of onset does not indicate whether one is dealing with embolism or thrombosis, since thrombosis may set in with severe acute symptoms and embolism may produce only intermittent claudication for a long time or no symptoms depending on the size of the vessel and the collateral circulation. The authors think that the departure from the classic clinical syndrome in six of their seven cases were probably due to (1) differences in the rate of progression of the occlusion, (2) the presence of an adequate collateral circulation and (3) subsequent development of a more efficient anastomotic circulation.

American Journal of Pathology, Boston

16:375-524 (July) 1940

Cardiac Lesions in Libman-Sacks Disease: Consideration of Its Relationship to Acute Diffuse Lupus Erythematosus. L. Gross, New York.—p. 375.
Histologic Changes in Ischemic Kidney, with Special Reference to Juxtaglomerular Apparatus. N. Goormaghtigh, Ghent, Belgium.—p. 409.
Histogenesis of Induced Pulmonary Tumors in Strain A Mice. H. G. Grady and H. L. Stewart, Bethesda, Md.—p. 417.
Histologic Lesion in Lymph Nodes in Infectious Mononucleosis. E. A. Gall and H. A. Stout, Boston.—p. 433.
Splenic Reticulum Cell Tumors in Mice. J. Furth and N. Krumdieck, New York.—p. 449.
Transmissible Malignant Neoplasm of Mice Originating in Reticular or Endothelial Cells. W. A. Barnes and J. Furth, New York.—p. 457.
Primary Encephalomyelitis in Goats Associated with Listerella Infection. L. S. King, Princeton, N. J.—p. 467.
Solitary Granuloma of Bone Simulating Primary Neoplasm. S. Otani and J. C. Ehrlich, New York.—p. 479.
Effects of Ovariectomy and Long Continued Administration of Anterior Pituitary Extract of Cattle on Skeletal Tissues of Immature Guinea Pigs. M. Silberberg and Ruth Silberberg, St. Louis.—p. 491.
Effect of Thyroidectomy and Administration of Anterior Pituitary Extract of Cattle on Growth of Cartilage and Bone of Immature Guinea Pigs. M. Silberberg and Ruth Silberberg, St. Louis.—p. 505.

Annals of Internal Medicine, Lancaster, Pa.

14:1-200 (July) 1940

*Clinical Application of Thiochrome Reaction in Study of Thiamine (Vitamin B_1) Deficiency. H. J. Borson, San Francisco.—p. 1.
Vitamin Deficiencies in Gastrointestinal Disease. T. T. Mackie, W. H. Eddy and M. A. Mills, New York.—p. 28.
Relation Between Clinical Edema and Excretion of Antidiuretic Substance in Urine. F. H. Robinson Jr. and L. E. Farr, New York.—p. 42.
*Treatment of Chronic Ulcerative Colitis with Sulfanilamide. E. N. Collins, Cleveland.—p. 55.
Concerning Correlation of Pathology and Symptoms of Coronary Artery Disease. F. M. Smith, Iowa City.—p. 65.
Malarial Coma. C. H. Sanford, P. T. Crawford and O. S. Warr Jr., Memphis, Tenn.—p. 72.
Effect of Oxalic Acid Intravenously on Blood Coagulation Time in Three Hemophiliacs. R. C. Page, H. K. Russell and R. L. Rosenthal, New York.—p. 78.
Prevention of Arthritic Deformities by Early Orthopedic Management. J. P. Stump, New York.—p. 87.
Cardiac Aneurysm: Report of Ten Cases. W. Dressler, New York, and R. Pfeiffer, Vienna, Austria.—p. 100.
Studies in Metabolism of Dextrose Fragments in Man. Frances F. Beck, Ruth Musser, C. J. Carr and J. C. Krantz Jr., Baltimore.—p. 122.
Treatment of Pneumococcic Pneumonia with Sulfapyridine. K. G. Kohlstaedt and I. H. Page, Indianapolis.—p. 129.
The American Board of Internal Medicine After Four Years; Organization, Purposes and Effects of Special Boards on Medical Education and Practice. E. E. Irons, Chicago.—p. 146.

Thiochrome Reaction and Thiamine Deficiency.—Borson outlines a modification of the thiochrome reaction of Jansen which provides an easy, rapid and accurate method for the chemical assay of thiamine (vitamin B_1) in urine. Subjects taking a diet adequate in thiamine excrete from 100 to 300 micrograms of thiamine daily. Of a standard oral test dose of 0.1 mg. per kilogram of weight from 8 to 10 per cent is excreted; most of the excess is found in the first five hours. The utilization of thiamine supplements depends in part on the degrees of absorption and excretion; large oral doses are incompletely absorbed and large parenteral doses are rapidly excreted. Therefore small frequent doses are utilized most efficiently. Excretion reflects intake with great sensitivity, even slight degrees of subsaturation being easily detected. The extent of deficiency may be estimated by determining the number of test doses required for the excretion to rise to normal. In patients with severe thiamine deficiency the total amount required for the excretion to become normal was tentatively estimated at about 100 mg. Evidence is presented that thiamine is a nonthreshold substance. Diuresis may wash out a considerable amount, thus contributing to the development of deficiency. The excretion in diffuse liver disease may be much higher than normal. This is interpreted as evidence that the ability to phosphorylate thiamine for utilization and storage is impaired. Moderate deficiencies found in patients with thyrotoxicosis despite diets containing fair amounts of "protective foods" may be explained by the increase in the metabolic rate and the consequent increase in the thiamine requirement. Several patients with "neuritis" of uncertain origin, having significant deficiencies, experienced definite relief after thiamine feeding. This indicates that thiamine deficiency played a part in the etiology, although typical thiamine deficiency disease was not present. Marked subsaturation occurred in 50 per cent of patients with multiple sclerosis and 29 per cent experienced definite symptomatic improvement after the oral administration of thiamine. The deficiency probably was secondary as the primary disease was not influenced by the treatment. Deficiencies were found frequently in patients with dorsolateral sclerosis and miscellaneous diseases of the central nervous system. Eighty per cent of patients with central nervous system syphilis were found to be undersaturated with thiamine; 58 per cent were definitely improved following pure thiamine therapy. There appears to be a definite indication for thiamine as a therapeutic measure in tic douloureux. Long-continued administration may be necessary in some patients before improvement will begin. Thiamine feeding was curative in a patient with nonspecific diarrhea, who also recovered from an idiosyncrasy to milk. Thiamine deficiency was frequent in patients with mild degrees of chronic disease of various types. Symptoms which are attributed to the primary disease or to "functional" disorders may be present in these patients and, because the classic picture of deficiency disease is absent, diagnosis can be made only by the therapeutic test. By estimating

the urinary excretion, asymptomatic deficiencies can be readily discovered and the test placed on a sounder basis in the diagnosis of deficiencies associated with symptoms.

Sulfanilamide for Chronic Ulcerative Colitis.—Collins appraises the use of sulfanilamide in the treatment of thirty-three cases of ulcerative colitis, azosulfamide in five and azosulfamide subsequent to sulfanilamide in six. The type treated corresponds to that described by Bargen and Buie as "thrombo-ulcerative colitis." The process was diffuse, inflammatory, destructive and hyperplastic, seen at proctosigmoidoscopic examination, while x-ray examination showed it to extend toward the colon. Sulfanilamide was given by retention enema not exceeding 45 grains (3 Gm.) in twenty-four hours. If the drug is well tolerated it is used for from ten to fourteen days and then on alternate weeks for two or three months with an interval of rest of from one to three months after each course, depending on the clinical course and the results. The enemas are given four times a day but not close to mealtime because of the gastrocolic reflex. Because of the tendency of the disease to recur it is important to use the drug in intermittent courses even after there is no evidence of activity. Since azosulfamide became available, its lower toxicity to sulfanilamide has been established and it has been given only by mouth, a total of 75 grains (5 Gm.) in five divided doses in twenty-four hours. The initial period of use and its intermittent use thereafter are similar to that of sulfanilamide. With continued improvement the daily dosage is reduced and the periods without the drug are lengthened. A complete and continued remission has occurred in eight, or 60 per cent, of thirteen nontoxic cases. In several instances it has lasted over more than two years. In ten (76 per cent) sulfanilamide was considered valuable and was the only treatment used. Further sulfanilamide proved to be of significance in producing favorable responses in fifteen of twenty-six nontoxic and toxic cases, or 57 per cent. Death occurred in four instances subsequent to the use of sulfanilamide. All four patients had extensive, if not irreparable, damage to the entire colon and were severely toxic at the time of admission. Multiple perforations of the colon were found at the time of operation in two patients; the third patient was 76 years of age and died after an operation for prostatic obstruction. Sulfanilamide was administered to the fourth patient for only six days. Ileostomy has been performed on three other severely toxic patients after sulfanilamide therapy failed. In combining these three cases with ten toxic cases in which medical management was employed, a remission attributable to sulfanilamide occurred in only four, or 30 per cent, of this group. Sulfanilamide has a place in the treatment of chronic ulcerative colitis and should be considered an adjunct to the usual forms of treatment and not as a specific remedy. It has proved of greatest value in the early nontoxic stage of the disease.

Archives of Internal Medicine, Chicago

66:295-530 (Aug.) 1940

Significance of Albumin-Globulin Ratio of Serum. D. Melnick, H. Field Jr. and C. G. Parnall Jr., Ann Arbor, Mich.—p. 295.
Practical Method for Measurement of Glomerular Filtration Rate (Inulin Clearance), with Evaluation of Clinical Significance of This Determination. A. S. Alving and B. F. Miller, Chicago.—p. 306.
*Purpura Haemorrhagica Due to Arsphenamines: Sensitivity in Patients as Influenced by Vitamin C Therapy. E. H. Falconer, N. N. Epstein and Edith S. Mills, San Francisco.—p. 319.
Dermatomyositis and Systemic Lupus Erythematosus: II. Comparative Study of Essential Clinicopathologic Features. H. Keil, New York.—p. 339.
Arteritis of Temporal Vessels: Report of Case. J. M. Bowers, Seattle.—p. 384.
Body Build and Hypertension. S. C. Robinson and M. Brucer, Chicago.—p. 393.
*Diagnosis and Treatment of Gonorrheal Septicemia and Gonorrheal Endocarditis. J. S. Davis Jr., New York.—p. 418.
Bacterial Endocarditis and Syphilis of Aortic Valve. D. H. Rosenberg, Chicago.—p. 441.
Survey of Diabetes: Statistical Data and Control Comparisons with Various Insulins. B. Smith and W. H. Grishaw, Los Angeles.—p. 465.
Infectious Diseases: Review of Significant Publications in 1939-1940. H. A. Reimann, Philadelphia.—p. 478.

Purpura from the Arsphenamines.—Falconer and his co-workers studied the effects of arsphenamines on seven patients who had toxic reactions accompanied by thrombopenic purpura following arsphenamine therapy. These patients have submitted to further injections, reproducing experimentally their attacks of purpura and affording an opportunity to study the effects of oral and parenteral administration of vitamin C on their sensitivity. Six of the patients were known to be sensitive to neoarsphenamine and only one to bismarsen. The previous reactions of these patients following each administration of neoarsphenamine or bismarsen varied from almost no symptoms in one to marked prostration, nausea, vomiting, rapid pulse, chills and malaise followed in each instance by thrombopenic purpura. Up to this time no vitamin C had been administered. The diet of each patient was inquired into carefully and the intake of vitamin C of only one patient was deemed inadequate. The amounts taken and the intervals during which the patients took vitamin C in crystalline form as ascorbic acid orally and intravenously varied considerably. It was impossible to standardize the sensitivity reaction to a given amount of the arsphenamine preparation causing a reaction. The variation of the reaction to different amounts of the drug was marked in the same patient at various time intervals. Variation in the different patients of the series was considerable and appeared as a distinctly individual characteristic. At no time and in no patient was there any appreciable modification of sensitivity reaction during or after the administration of vitamin C. An increase in severity of the reactions after administration of vitamin C in certain of the patients was probably due entirely to increased sensitivity as the result of previously administered arsphenamine.

Gonorrheal Septicemia and Endocarditis.—Davis believes that a discussion of gonorrheal septicemia and endocarditis is timely because the condition apparently is not uncommon. The diagnosis is either missed or not made until after death at postmortem examination and because fever therapy, sulfanilamide and its derivatives are means with which the infections may be combated. The data of fourteen cases, with four recoveries, are reported. Thirteen cases were thought to be endocarditis and one a pericarditis. Two of the patients were seen by the author. The patients who recovered were not proved definitely to have gonorrheal septicemia, but the author gives the following fourteen points which in his case he believes should substantiate such a diagnosis: a positive gonococcus complement fixation test, no petechiae, varying heart murmurs from day to day, no change in conduction time of the heart as would be expected in a rheumatic infection, indication after bouts of pneumonia that the invading organism was sensitive to heat, fluid removed from the cavity in the chest cloudy and apparently sterile (similar observations are made in gonorrheal pleurisy), a history of a severe previous attack of gonorrhea and recent alcoholic and sexual excesses, recovery following multiple blood transfusions and Corbus-Ferry filtrate therapy, five attacks of pneumonia which was probably embolic, the presence of jaundice probably due to hemolysis, a palpable spleen, gallop rhythm on three occasions, severe abdominal pain (probably embolic in character) for which an exploratory operation was performed and evidence of renal infarct. Death in this disease is often of renal origin. The diagnosis is simple in those cases in which the acute disease follows trauma to the urethra in the course of therapy for acute gonorrhea. The author believes that if his foregoing observations are kept in mind an earlier diagnosis may be made, which will prevent useless major operations and explorations of the chest and will hasten the patient's recovery. If sulfanilamide or fever therapy could be used early in the disease, the mortality could be much reduced. A study of the data reveals (1) the difficulty in establishing a definite diagnosis, which is often not made until after death, (2) the frequent occurrence of pneumonia, (3) the infrequency of petechiae and the peculiarity of the cutaneous lesion, (4) the difficulty attendant on obtaining a positive blood culture and (5) the fact that recovery is possible. Accepted forms of treatment seem to be (1) sulfanilamide up to 150 grains (10 Gm.) daily, (2) artificial fever induced by the Kettering hypertherm, (3) blanketing the patient, thus utilizing the patient's body heat to maintain a fever, (4) multiple blood transfusions and (5) surgical removal of any focus of infection (frequently never found even at necropsy). Sulfanilamide must be given with great caution so as not to deplete the leukocytes and erythrocytes.

Archives of Ophthalmology, Chicago

24:221-438 (Aug.) 1940. **Partial Index**

*Methods for Visual Testing in Schools. J. B. Hitz, Milwaukee.—p. 221.
Site of Disturbance in Adie's Syndrome. H. G. Scheie, Philadelphia.—p. 225.
Phi Phenomenon and Anomalous Projection. F. H. Verhoeff, Boston.—p. 247.
Clinicopathologic Study of Diabetic Retinitis. S. A. Agatston, New York.—p. 252.
Studies of Visual Fields in Connection with Tryparsamide Therapy. L. S. Powell, Lawrence, Kan., and H. S. Smith, Osawatomie, Kan.—p. 276.
Local Action of Oils Containing Vitamin A: Experimental Contribution. A. de Rötth, Spokane, Wash.—p. 281.
More Nearly Absolute Method of Testing and Rating Vision. C. E. Ferree and G. Rand, Baltimore.—p. 292.
Studies in Convulsant Therapy: IV. Effects of Metrazol (Pentamethylenetetrazol) on Eye. S. R. Dean, Newtown, Conn.—p. 316.
Acute Hydrops of Cornea Complicating Keratoconus. R. O. Rychener, Memphis, Tenn., and D. B. Kirby, New York.—p. 326.
Ocular Sensitivity to Nupercaine. C. A. Perera, New York.—p. 344.
Vaccinal Disciform Keratitis Following Accidental Inoculation of Eyelid. C. A. Perera, New York.—p. 352.
Rhinosporidiosis of Conjunctiva. H. D. Barnshaw and W. T. Read Jr., Camden, N. J.—p. 357.
Vaccinia of Eyes. J. Laval, New York.—p. 367.
Pathologic Conditions of Cornea: I. Disturbances of Epithelium, Endothelium and Bowman's and Descemet's Membrane. B. Rones, Washington, D. C.—p. 374.

Methods for Visual Testing in Schools.—Hitz compared the results of the Snellen chart test, the Betts test and a group of tests (hereafter referred to as the author's tests) consisting of the Snellen chart at 6 meters, the Duane screen test at 6 meters and 33 cm. and the Worth four dot test at 6 meters and 33 cm. The tests were performed by lay examiners on 745 average school children between the ages of 8 and 16. None of the tests were to be considered diagnostic but merely a means of determining which children should be referred to an ophthalmologist for a complete examination. The percentages of those who passed and failed were, respectively, Snellen test 89.7, 10.3; Betts test (the Betts method of grading) 17.4, 82.6; Betts test (the Davenport, Iowa, method of grading) 58.4, 41.6, and his group of tests 55.4 and 44.6. It seems obvious that any test which finds 82 per cent of school children with defective vision is too discriminating and defeats its own purpose. If such were the case it would be more sensible to refer all children to an ophthalmologist and eliminate screen testing. The figures further suggest that the Snellen test alone is missing a considerable number of muscular and fusional difficulties. A comparison of the results obtained with the Snellen test with those obtained with the Betts visual acuity test shows the Betts test to be slightly more discriminating. A comparison of the results of the fusion tests with those of the four dot test reveals that the Betts test again shows the greater percentage of failures. A comparison of the results of the muscle balance tests with those of the Betts test shows that the Betts test reveals more failures. A criticism of the Betts test is that the time consumed in examining the individual person is almost double that with his group of tests. The author believes that his group of tests would seem to strike a mean between the other two tests considered. The tabulated results warrant the conclusion that the tests in present use are either inadequate or overzealous and that a further effort toward the development of standard visual efficiency tests to be used in the nation's schools should be made.

Arkansas Medical Society Journal, Fort Smith

37:57-74 (Aug.) 1940

Convalescent Serum in Prophylaxis and Treatment of Communicable Diseases. S. G. Wolfe, Shreveport, La.—p. 57.
Management of Normal Labor. G. L. Kimball, DeQueen.—p. 62.

Bulletin New York Academy of Medicine, New York

16:501-552 (Aug.) 1940

Features Which Suggest Public Health Consideration of Rheumatic Fever. H. F. Swift, New York.—p. 501.
Clinical Aspects of Rheumatic Fever in Adults. I. R. Roth, New York.—p. 514.
Management of Anemias in Infancy and Childhood. C. H. Smith, New York.—p. 525.
Convalescence in Coronary Disease, with Special Reference to the Saratoga Spa Therapy. C. R. Comstock, Saratoga Springs, N. Y.—p. 546.

Johns Hopkins Hospital Bulletin, Baltimore

67:79-162 (Aug.) 1940

Retinal Arteries in Experimental Renal Hypertension: Significance of Localized Caliber Constriction. R. C. Laughlin, Caroline Bedell Thomas and J. S. Friedenwald, Baltimore.—p. 79.
Toxin Antitoxin Reactions in Experimental Tetanus. H. B. Shumacker Jr., W. M. Firor and A. Lamont, Baltimore.—p. 92.
Studies in Thiamine Excretion. V. A. Najjar and L. E. Holt Jr., Baltimore.—p. 107.
Functional Studies Following Lesions of Cerebellar Vermis Involving Nucleus Fastigii. R. S. Snider.—p. 125.
Functional Studies Following Lesions of Nucleus Interpositus in Rabbit. R. S. Snider.—p. 139.

Journal of Nutrition, Philadelphia

20:99-196 (Aug.) 1940. **Partial Index**

Ascorbic Acid Content of Goat's Milk and Blood: Influence of Ascorbic Acid Injection and Diet. Martha S. Richmond, G. H. Satterfield, C. D. Grinnells and W. J. Dann, Raleigh and Durham, N. C.—p. 99.
Effect of Complementing Factors on Quantitative Response and Specificity of Vitamin B6. G. C. Supplee, R. C. Bender and O. J. Kahlenberg, Bainbridge, N. Y.—p. 109.
Cereals and Rickets: XII. Effect of Calcium and Vitamin D on Availability of Phosphorus. C. H. Krieger and H. Steenbock, Madison, Wis.—p. 125.
Effects Produced by Decreasing Calcium and Phosphorus Intake on Calcium and Phosphorus Absorption and Deposition and on Various Bodily Constituents of Rat. G. Bachmann, J. Haldi, W. Wynn and C. Ensor, Emory University, Ga.—p. 145.
Biologic Assay of Riboflavin in Liver of Cow, Calf, Sheep, Lamb and Hog. Olga B. Saffry, Hazel S. Cox, Bernice L. Kunerth and Martha M. Kramer, Manhattan, Kan.—p. 169.
Histologic Studies of Tissues of Rats Fed Diet Extremely Low in Phosphorus. R. H. Follis Jr., H. G. Day and E. V. McCollum, Baltimore.—p. 181.

New England Journal of Medicine, Boston

223:205-238 (Aug. 8) 1940

Surgical Treatment of Carcinoma of Prostate. J. A. C. Colston, Baltimore.—p. 205.
Riboflavin Deficiency: Report of Case in Child with Cure by Specific Treatment. W. P. Shields, Providence, R. I.—p. 215.
Erythema Multiforme Bullosum with Involvement of Mucous Membranes of Eyes and Mouth (Stevens-Johnson Disease): Report of Case. H. Ageloff, New York.—p. 217.
Pharmacology. G. P. Grabfield, Boston.—p. 220.

223:239-264 (Aug. 15) 1940

Hypovitaminosis of All Fat Soluble Vitamins Due to Steatorrhea: Report of Case. F. Albright and J. D. Stewart, Boston.—p. 239.
*Recovery from Acute Rheumatic Fever Without Permanent Cardiac Damage. M. G. Brown and L. Wolff, Boston.—p. 242.
Infections of Upper Urinary Tract in Diabetic Patient. A. D. Baldwin and H. F. Root, Boston.—p. 244.
Radiation Therapy. R. Dresser, Boston.—p. 250.

Recovery from Rheumatic Fever Without Cardiac Damage.—This study by Brown and Wolff is based on 175 consecutive unselected cases of acute rheumatic fever, with or without chorea. Only cases in which the diagnosis was clear were included. Following the acute attack they were seen in the cardiac clinic of the outpatient department on repeated occasions over periods varying between four and eleven years, and most of them were seen for the final evaluation of their cardiac status. In arriving at the final opinion, the physical examination, the electrocardiogram, the 7 foot roentgenogram of the heart and the fluoroscopic examination for chamber enlargement were taken into consideration. In this series there were eighty-nine patients who developed or already had valvular damage as a result of rheumatic fever. Patients presenting loud and constant systolic murmurs as the only cardiac abnormality were included in this group. The remaining eighty-six cases were divided into three groups. Group 1 included twenty-one patients who at no time showed murmurs or other evidence of cardiac involvement. Group 2 consisted of twenty-nine patients in whom, at the time of rheumatic activity, murmurs and other evidences of cardiac involvement were present but subsequently disappeared. Group 3 included thirty-six patients who showed a persistent but inconsequential systolic murmur. The present study confirms the known fact that some patients with acute rheumatic fever escape permanent organic valvular damage. The proportion of those escaping permanent cardiac damage is higher in this series (50 per cent) than in any other published series. It is generally believed that, the more severe the infection or the greater the number of recurrences, the more apt is the patient to develop perma-

nent cardiac injury. This belief is not substantiated by the observations here reported. The rheumatic infection in the patients who recovered without permanent heart disease was no different clinically from that in the others. There was no difference in the duration. Of the eighty-six patients who escaped permanent cardiac damage, forty-two had multiple attacks of rheumatic fever. Thus patients who recover without permanent organic heart changes from a first attack seem to have an excellent chance of doing so from subsequent ones. This conclusion is of prognostic and therapeutic significance and makes possible the less rigid restriction of activity of certain patients during subsequent attacks of active rheumatic infection. The final evaluation of the state of the valves must be delayed for several years after an attack of rheumatic fever.

Physiological Reviews, Baltimore

20:313-468 (July) 1940

Carbon Monoxide Anoxemia. Esther M. Killick, London, England.—p. 313.
Fluctuations in Body Iodine. W. T. Salter, Boston.—p. 345.
Role of Potassium in Physiologic Processes. W. O. Fenn, Rochester, N. Y.—p. 377.
Porphyrins in Health and Disease. K. Dobriner and C. P. Rhoads, New York.—p. 416.

Public Health Reports, Washington, D. C.

55:1327-1370 (July 26) 1940

Protective Ointment for Prevention of Poison Ivy Dermatitis. L. Schwartz, L. H. Warren and F. H. Goldman.—p. 1327.
Effect of Synthetic Pantothenic Acid on Adrenal Hemorrhage, Atrophy and Necrosis in Rats. F. S. Daft, W. H. Sebrell, S. H. Babcock Jr. and T. H. Jukes.—p. 1333.
Effect of Administration of Pantothenic Acid on Histopathology of Filtrate Factor Deficiency State in Rats. L. L. Ashburn.—p. 1337.

55:1371-1418 (Aug. 2) 1940

Disease Outbreaks Resulting from Faulty Environmental Sanitation. L. C. Frank.—p. 1373.
Report on Market-Milk Supplies of Certain Urban Communities.—p. 1383.
Susceptibility and Resistance of Certain Species of American Deer Mice, Genus Peromyscus, and Other Rodents to Leptospira Icterohaemorrhagiae. A. Packchanian.—p. 1389.
Disabling Morbidity Among Male and Female Industrial Workers During 1938 and 1939, and Among Males During the First Quarter of 1940, with Inquiry into Occurrence of Multiple Attacks of Disabling Sickness and Injuries, 1939. W. M. Gafafer.—p. 1402.

Radiology, Syracuse, N. Y.

35:131-260 (Aug.) 1940

Clinical and Pneumo-Encephalographic Studies in Presenile Dementia. J. Romano and W. C. Miller, Boston.—p. 131.
Radiologic Society of North America Standardization Committee, Technical Bulletin No. 1. Edith H. Quimby and G. C. Laurence.—p. 138.
*Familial Lumbosacral Syringomyelia. C. Van Epps and H. D. Kerr, Iowa City.—p. 160.
The New Alchemy. M. A. Tuve, Washington, D. C., with added remarks by R. R. Newell, San Francisco.—p. 174.
Use of Artificially Produced Radioactive Elements as Tagged Atoms in Biologic Research. W. F. Bale, Rochester, N. Y.—p. 184.
Treatment of Radiation Reactions Following 200 Kilovolt Therapy. Zoe Allison Johnston, Pittsburgh.—p. 192.
Physical Factors of Low Voltage "Contact" Roentgen Therapy. C. B. Braestrup and I. H. Blatz, New York.—p. 198.
Normal Bone Angles and Roentgen Report. R. G. Van Nuys, Berkeley, Calif.—p. 206.
Further Studies on Effects of Irradiation on Proliferation and Metabolic Processes of Normal and Malignant Tissues: IV. Effects Produced by Different Dosage Rates of X-Ray Radiation on Proliferation of Various Tissues Grown in Vitro. Anna Goldfeder, New York.—p. 210.
Additive Effects of Radon and Neutral Red on Chaos Chaos. Vera Koehring, Boston.—p. 229.
"Know Thyself." R. E. Myers, Oklahoma City.—p. 236.

Familial Lumbosacral Syringomyelia.—The appearance at their clinic of two or more members of four different families with trophic changes in the soft and bony tissues of the feet led Van Epps and Kerr to review the literature of similar cases. It is their belief that the various etiologic factors of the syndrome are of the developmental type and that the terms status dysraphicus, myelodysplasia, syringomyelia and trophopathia pedis myelodysplastica all have some basis. They have classified their cases in the syringomyelia group and feel that the term "familial lumbosacral syringomyelia" is the best term. To date there have been reported fifty-four cases, to which the authors now are adding twenty-seven of their own, making a total of eighty-one cases. They have examined nineteen of the twenty-seven included in this report. Twenty-six of these cases occurred in four families, while in the other case the authors have been unable as yet to establish a familial tendency. Of the nineteen examined cases the feet showed calluses in sixteen, one or more ulcers in seventeen and pain, usually slight, in six. The knee jerks were normal in eighteen, the achilles tendon reflex was absent in twelve and plantar extension was absent in one or both feet in nine. Pallesthesia was impaired or lost in sixteen, hyperkeratosis was present in the hands in two cases, and the skin of the hands was dry and thick in a third case. X-ray examination of the feet showed osseous changes in fifteen cases. These changes were trophic in character—absorption of bone, disintegration of joints, periosteal new bone and pathologic fractures. Soft tissue changes could also be seen. Films of the lumbosacral spine convinced the authors that spina bifida occulta per se is not a necessary part of the syndrome. In four cases there were episodes of severe infection. One case of chronic infection necessitated amputation below the knee. In only one case has there been a possible appearance of the condition in the fourth generation. One family showed an associated case of striate diplegia with athetosis. The sporadic case showed unequal partial Argyll Robertson pupils, primary optic atrophy, and retrobulbar neuritis with slightly constricted fields. This case may be one of tabes, but the authors have included it because they have not seen similar changes in the feet occurring in tabes and because these changes are typical of those in the familial groups. They reach the conclusion that the occurrence of chronic painless ulcers on the feet, especially when associated with x-ray evidence of neurotrophic changes in the bones and joints of the forefeet, should lead to a study of the family history in a search for similar cases. Familial lumbosacral syringomyelia is one of the most frequent causes for such a syndrome. Irradiation of the lumbosacral cord appears to be the best available treatment.

Rocky Mountain Medical Journal, Denver

37:553-636 (Aug.) 1940

Chronic Gastritis. R. Schindler, Chicago.—p. 570.
Industrial Hygiene. R. R. Sayers, Washington, D. C.—p. 576.
Tuberculosis in Industry. D. E. Cummings, Saranac Lake, N. Y.—p. 579.

Texas State Journal of Medicine, Fort Worth

36:277-342 (Aug.) 1940

Iron Requirements in Childhood and Adult Life. F. J. Heck, Rochester, Minn.—p. 286.
Hippuric Acid Synthesis Test for Liver Function. D. L. Curb, Galveston.—p. 292.
Metrazol and Insulin Treatment in Psychiatry. A. J. Schwenkenberg and R. E. Winn, Dallas.—p. 296.
Diagnostic and Prognostic Value of Sedimentation Rate. L. C. Kopecky, San Antonio.—p. 302.
Space-Occupying Lesions of Spinal Canal. J. Greenwood Jr., Houston.—p. 305.
Sulfanilamide in Urology. C. M. Simpson, Temple.—p. 311.
How Does the Follicle Reach the Ovarian Surface? E. O. Strassmann, Houston.—p. 313.
Tuberculous Uveitis: Case Report. M. Thomas, Dallas.—p. 319.
Philosophy of the New Deal, a World Problem: A Doctor's Point of View. W. B. Russ, San Antonio.—p. 323.

Virginia Medical Monthly, Richmond

67:465-524 (Aug.) 1940

Incidence of Pulmonary Tuberculosis in Southwestern State Hospital: Preliminary Report. J. R. Blalock, J. B. Funkhouser and J. E. K. Flannagan, Marion.—p. 465.
Present Status of Serodiagnostic Tests for Syphilis from the Standpoint of the Clinician. D. C. Smith, Charlottesville.—p. 469.
Syphilis in the Pregnant Woman. W. McMann, Danville.—p. 473.
Bipartite Patella. J. L. Tabb, D. M. Faulkner and C. D. Smith, Richmond.—p. 475.
Pyrus Malus, Belonging to Suborder of Pomaciae, of the Natural Order Rosaceae. W. O. Bailey, Leesburg.—p. 479.
Ruptured Intervertebral Disk and Hypertrophied Ligamentum Flava Follow-Up Study. H. L. Skinner, Baltimore.—p. 490.
Sulfapyridine: Uses and Report of Cases. R. H. Temple, Kinston, N. C.—p. 494.
Tuberculosis, Review and Local Study: Five Year Study of Clinic Patients in a City of 34,500 Population. T. N. Hunnicutt Jr., Newport News.—p. 500.
Eosinophilia: Report of Atypical Case. R. D. Garcin Jr., Richmond.—p. 507.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Heart Journal, London

2:141-220 (July) 1940

Peripheral Circulation by Photoelectric Recording. B. Leibel.—p. 141.
Regeneration in Cardiac Muscle. E. S. J. King.—p. 155.
*Tuberculous Pericarditis. H. L. Heimann and S. Binder.—p. 165.
Right Ventricular Hypertrophy of Unknown Origin: So-Called Pulmonary Hypertension. S. de Navasquez, J. R. Forbes and H. E. Holling.—p. 177.
Pulmonary Hypertension. T. East.—p. 189.
Failure of Right Ventricle: Case Report. T. G. Armstrong.—p. 201.
Coarctation of Aorta At or Above Origin of Left Subclavian Artery. R. H. Bayley and J. E. Holoubek.—p. 208.
Paroxysmal Tachycardia Caused by Pentamethylene Tetrazol. F. Klein.—p. 213.

Tuberculous Pericarditis.—According to Heimann and Binder, tuberculous pericarditis is not a rare primary clinical manifestation among Bantu people. Observation over fifteen years in the non-European hospital revealed thirty-one cases; some were of the constrictive type which is amenable to operative treatment and some were only part of a generalized tuberculemia; there were none of the healed constrictive type. The finding of a large "pericardial-shaped heart" in a Bantu justifies a clinical diagnosis of tuberculous pericarditis when rheumatic manifestations and evidence of mitral and aortic disease are absent. Tuberculous root glands were present in all the cases. The tuberculous process was localized to the root glands and pericardium in ten. In six the lungs, pericardium and root glands were tuberculous. Terminal miliary tuberculosis occurred in twelve: in eight following primary root gland and pericardial tuberculosis and in four following primary lung, root gland and pericardial tuberculosis. Pleural effusions were present in fifteen cases, being bilateral in most; in eleven there was either an acute pleurisy or pleural adhesions. Chronic congestion of the liver was present in most with either fibrous, fatty or tuberculous changes. In spite of the short duration of the history, usually between three and six months, the authors believe that the condition is usually insidious in its onset and that these Bantu patients began to notice symptoms only when they became severe. A history typical of congestive cardiac failure was generally given, especially in cases of the effusion type. Usually there was complaint of cough. Hemoptysis occurred in five cases. Seventeen patients complained of abdominal pain, usually localized to the right hypochondrium, and eleven complained of chest pain, usually localized to the precordium. Edema of the legs was observed in eleven, breathlessness in eleven and loss of weight in eleven. The temperature was raised in twenty-two, the respiratory rate in twenty and the pulse rate in twenty-nine. A febrile chart, rapid pulse and breathlessness were found chiefly with pericardial effusions. Most of the patients were poorly nourished; fifteen had an emaciated appearance. Signs of pulmonary tuberculosis were present in only nine patients. The tuberculosis was of the primary clinical type of Riesman (1901). The liver was enlarged and tender in twelve, and eight had ascites. The effusion stage is the easiest one in which to make a clinical diagnosis; the enlarged pear-shaped area of cardiac dulness with an obtuse cardiohepatic angle is the main sign. Death usually occurred in from one to six months after the onset of symptoms. Pericardial aspiration and pneumopericardium improve the prognosis as far as the time of survival is concerned. This is substantiated by the fact that in the only patients who left the hospital the pericardium had been aspirated and in addition pneumopericardium was performed in one. The cause of death is either cardiac failure or, more commonly, miliary tuberculosis, which is common in tuberculous pericarditis. The probable entry of the organisms into the blood stream, particularly in cases in which there is intrapericardial caseation, is by the rupture of a tuberculous follicle into a vein.

Journal of Laryngology and Otology, London

55:269-302 (June) 1940

*Tuberculosis of Larynx in Childhood. T. O. Howie.—p. 269.

Tuberculosis of Larynx in Childhood.—Howie looked for laryngeal lesions when examining 159 children, from 4 months to 16 years of age, suffering from pulmonary tuberculosis. Tubercle bacilli were present in the sputum or in the stomach washings of ninety of these. Thirty-eight of the "open" cases presented tuberculous laryngeal lesions. Tuberculous laryngeal disease was present in only three cases with sputums or stomach contents negative for tubercle bacilli. It appeared that bovine and human infection is equally prone to produce laryngeal disease. Most of the lesions occur in open cases with cavitation and bronchopneumonic pulmonary lesions. Postmortem examination of specimens confirmed this observation. The youngest child to have tuberculosis of the larynx was an infant of 4 months. He died with multiple lesions in the mastoid, the kidney and the intestine. The lungs showed extensive bronchopneumonic disease. In the early stages of laryngeal involvement there is seldom any indication of its presence. The child makes no complaint of discomfort, pain or hoarseness unless the cords are destroyed or kept apart by the bulk of tissue during phonation. Even when the condition has advanced to the stage of perichondritis of the arytenoid or epiglottis there is no complaint of pain. Dysphagia was not encountered. The tuberculous laryngeal lesions conformed to those seen in adults, varying from a slight "streaking" of one cord to extensive destruction of the larynx, with perichondritis and fetid breath. The presence of some of these lesions was confirmed at necropsy. They were usually located in the posterior part of the larynx, in the interarytenoid area and on the posterior extremity of the cords. The disease usually began with a peaking in the interarytenoid area and was followed by destruction of one or both cords over the vocal process of the arytenoid. A few progressed to the stage of tuberculous papillomatosis. When a lesion developed during the interval of six weeks which elapses between examinations of all children, vocal rest and creosote inhalation have in many instances led to a resolution of the condition. The laryngeal condition runs parallel to the pulmonary condition. If the general condition becomes worse the laryngeal condition likewise gets worse. If marked improvement occurs in the former, as it often does after successful pneumothorax treatment, there is a tendency for the latter to be arrested and in some cases to resolve. Possible routes of infection are discussed. The author believes that the cases reported here provide evidence that laryngeal involvement is the result of direct implantation of tubercle bacilli in the tissues of the larynx.

Lancet, London

2:123-154 (Aug. 3) 1940

Treatment of Gunshot Wounds of Peripheral Nerves. H. Cairns and J. Z. Young.—p. 123.
*Fibrin Suture of Peripheral Nerves: Measurement of Rate of Regeneration. J. Z. Young and P. B. Medawar.—p. 126.
*Nerve Regeneration: Importance of Peripheral Stump and Value of Nerve Grafts. J. Z. Young, W. Holmes and F. K. Sanders.—p. 128.
Small-Scale Filtration of Citrated Plasma. S. R. M. Bushby, G. A. H. Buttle and L. E. H. Whitby.—p. 131.
Postmortem Cesarean Section with a Living Child. Joyce Morgan.—p. 132.
Reduction of Dust-Borne Bacteria by Treating Floors. M. van den Ende, Dora Lush and D. G. f. Edward.—p. 133.
Head Tetanus: Case. E. C. B. Butler.—p. 134.
Koplik Spots in Colon. F. G. Hobson.—p. 134.

Fibrin Suture of Peripheral Nerves.—Young and Medawar present a method by which stumps can be held together with concentrated coagulated blood plasma. The method reduces the difficulties of nerve suture and minimizes the disorganization of fibers which is apt to be produced by stitches. It consists in holding the cut stumps together and pouring round them plasma which has been mixed with strong tissue-extract. In from one half to two minutes the plasma clots to a firm jelly which sticks to the nerves and holds the stumps together. The plasma is freely permeable and is dissolved away during the subsequent days, remaining, however, long enough to allow a firm union. The gel formed by ordinary plasma is not sufficiently strong to maintain union under tension, but it can be fortified by dissolving in it sufficient fibrinogen to increase its normal concentration. Cockerel plasma has proved more satisfactory than that of mammals. Blood is withdrawn from the carotid artery through oiled cannulas into large centrifuge tubes. These are packed in ice for ten minutes and then spun. The supernatant plasma is stored in waxed test tubes on ice and keeps for at least six weeks. The animal should be starved for thirty-six hours before. No heparin need be used. The concentration is effected by the precipitation of fibrinogen (with

prothrombin) from part of the plasma and by its re-solution in a smaller volume. The concentration thus concerns only the protein constituents. The method of salting out by half-saturation with sodium chloride is unsatisfactory, because the excess of salt interferes with clotting. Mellanby's method is used, one volume of plasma being mixed with nine volumes of redistilled water and then slowly with from 0.1 to 0.15 volume of a solution of acetic acid in redistilled water containing 1 per cent by volume. The fibrinogen forms a flocculate, which is centrifuged out after standing for five minutes. The supernatant fluid is discarded and replaced with water, which is also taken off with a fine pipet. The fibrinogen may now be either used directly or stored under distilled water at 4 C. It keeps for at least ten days. Before use the fibrinogen is dissolved in plasma—not in saline solution, because in the presence of serum the fibrin clot is stronger and much more stable. For use with rabbit nerves a six times normal concentration has proved satisfactory; that is, one produced by dissolving in one volume of plasma the fibrinogen precipitated from five volumes. The quick and even coagulation of the plasma is ensured by mixing it thoroughly just before application with not more than a tenth of its volume of a concentrated tissue-extract. Chicken-embryo extract in saline solution (2 cc. for a ten day embryo) is satisfactory. The plasma method has been found to give satisfactory junction of the cut sciatic nerve of the rabbit. Little or no plasma penetrates between the cut stumps, and no barrier to regeneration is presented. Microscopic study shows that the junctions made by the plasma method are readily crossed by nerve fibers. It is impossible in any nerve junction to ensure that all the fibers pass straight from the central to the peripheral stump, but in the fibrin junction there is a near approach to this condition, with none of the whorls and deviation of large bundles of fibers, which are unavoidable with stitching unless the epineurium alone is sutured—a difficult achievement with small nerves.

Nerve Regeneration.—Young and his associates point out that Cajal has established that recovery after section of a peripheral nerve depends on the outgrowth of new nerve fibers from the central stump but that there still remains some uncertainty about the contribution made by the peripheral stump. Knowledge regarding the peripheral stump is of importance in deciding on operation; e. g., the advisability of delay before suture, and the possibilities of nerve grafts. That the peripheral stump plays a part in making the junction is shown by experiments in which the nerves are cut and the stumps allowed to remain separate. Such operations have been done on rabbits. The rates of outgrowth observed from the central stumps vary from zero, in cases in which a bulb was formed, to a maximum of 0.4 mm. a day. The average rate of outgrowth was 0.2 mm. a day. This is much slower than the rate found for outgrowths from peripheral stumps, which send out strands at a rate of 0.45 mm. a day, and in some cases 1 mm. a day. The extent of these proliferations from peripheral stumps differs from animal to animal, and the authors have not been able to discover what variable factors are involved. It appears, however, that the Schwann cells grow best when they have some support, such as was provided by leaving a part of the sciatic nerve uncut. When the central and peripheral stumps are left close together with a gap less than about 2 cm., union between them may take place rapidly. The average rate for crossing such gaps was 0.77 mm. a day and the highest rate was 1.3 mm. a day. Though it is impossible to discover what proportion of the outgrowth comes from each of the stumps, there is reason to believe that the greater part comes from the peripheral end. The speed of outgrowth of Schwann cells from the peripheral stump suggests that there may be some accelerating and attracting influence exercised by the central stump on the Schwann tissue growing from the peripheral stump. There is no doubt that Schwann cells, growing mainly from the peripheral stump, can effectively bridge gaps between cut ends. The fact that outgrowth takes place so actively from a peripheral stump emphasizes the importance of the contribution made by the Schwann cells to regeneration, and proper appreciation of this is essential in considering the various types of graft for bridging defects. The difficulty in assessing the value of grafts is partly due to the fact that there has been no quantitative comparison. The authors made such a comparison by measuring the distance reached by outgrowing fibers after the insertion of grafts of various sorts into the peroneal nerve of the rabbit. The grafts were always pieces of rabbit tibial nerve 2 cm. long and were fixed in place under aseptic conditions with concentrated fibrinogen solutions. After from fifteen to twenty-five days the animal was anesthetized and the length of outgrowth determined by pinching the nerve from a distal point upward until a reflex response was obtained. Grafts of different sorts were placed on opposite sides of each rabbit. The authors made experiments with autografts, predegenerated autografts, homografts, stored homografts and alcohol-fixed homografts. It was found that a fresh autograft provides for the growth of new fibers a medium which is only slightly less satisfactory than a normal peripheral stump. Since it seems that successful regeneration depends on the active contribution of the living Schwann cells of the peripheral stump, it is essential that the graft be treated as a living thing and not pinched with forceps, dried or otherwise maltreated. Fresh autografts provide the most successful results, and predegeneration does not seem worth while. The success of the thin Ballance-Duel grafts suggests that small nerves may make better grafts than large nerves, and a cable graft of several thin strands is probably better than a single thick graft.

Medical Journal of Australia, Sydney

1:885-914 (June 29) 1940

Cerebral Compression: Clinical and Experimental Study. W. L. Reid. —p. 885.
Studies in Tuberculosis: VI. By Effects of Purified Protein Derivative of Tuberculin as Used for Mantoux Test. D. Anderson.—p. 893.
Cryptophthalmos or Ablepharia: Survey of Condition with Review of Literature and Presentation of Case. I. Brodsky and G. Waddy. —p. 894.

2:1-28 (July 6) 1940

Spinal Analgesia. A. D. Morgan.—p. 1.
Snake Bite in Practice. H. Flecker.—p. 8.
Technic of Intracutaneous Tuberculin Test. D. Anderson.—p. 13.

2:29-50 (July 13) 1940

Some Acute Virus Diseases of Respiratory System. E. W. Hurst.—p. 29.
Orthopedics and the Great War. L. O. Betts.—p. 35.

2:51-76 (July 20) 1940

Cerebrospinal Meningitis. W. L. Calov.—p. 51.

Practitioner, London

145:85-148 (Aug.) 1940

Prevention of Acute Specific Fevers. J. C. G. Ledingham.—p. 85.
Prevention of Pulmonary Tuberculosis. R. C. Wingfield.—p. 92.
Prevention of Mental Illness. R. G. Gordon.—p. 99.
Prevention of Dietary-Deficiency Diseases. L. J. Harris.—p. 105.
Prevention of Venereal Disease. R. Lees.—p. 119.
Treatment of Wartime Neuroses in Combatants. E. Bramwell.—p. 124.
Modern Therapeutics: XIV. Antipyretics. V. J. Woolley.—p. 132.

Tubercle, London

21:249-280 (May) 1940

Position of Transverse Interlobar Fissure of Lung in Relation to Prognosis in Pulmonary Tuberculosis. B. H. Y. T'Ang and C.-L. Hsu. —p. 249.
Pathogenesis of Tuberculosis of Peripheral Lymph Nodes: Clinical Study of 324 Cases. B. C. Thompson.—p. 260.

Chinese Medical Journal, Peiping

57:401-500 (May) 1940

Tuberose Sclerosis of Brain (Bourneville) and Adenoma Sebaceum of Face (Pringle) in a Chinese. I. Snapper.—p. 401.
Studies on Stability of Suspension for Agglutination of Corynebacterium Diphtheriae. C. H. Huang and R. H. P. Sia.—p. 418.
Pellagra Among War Refugees in Shanghai: Its Associated Deficiencies and Nicotinic Acid Treatment. H. H. Morris, M. S. Hwang and P. T. Kuo.—p. 427.
Notes on Kala-Azar Research in China: Part II. Use of "Distibinyl" in Treatment of Chinese Kala-Azar. C. J. Sun and S. Chang.—p. 442.
Dyspnea: Lecture in Applied Physiology. H. S. D. Garven.—p. 449.
Survey of Intestinal Parasites in Rural Szechwan. T. H. Williams. —p. 464.
Infectious Mononucleosis: Report of Case. J. B. Robinson.—p. 473.
Congenital Dislocation of Radius. C. M. Meng.—p. 479.
Treatment of Fracture of Patella by Excision. H. C. Chih.—p. 482.
Nonmetrical Study of Bony Nose of the Chinese. C. S. Lu.—p. 485.

Brasil-Medico, Rio de Janeiro

54:379-392 (June 1) 1940. **Partial Index**

*Influence of Heredity in Allergic Disease: Study of Familial Incidence in 350 Allergic Persons. A. de Oliveira Lima.—p. 379.
Practical Classification of Convulsions. J. Barbosa.—p. 383.

Heredity in Allergic Diseases.—De Oliveira Lima discusses the role of heredity in the development of allergic diseases and reports his observations on familial incidence in 350 cases of allergy in persons of either sex. There was a history of allergy in the parents or relatives of the patients in 289 cases. It was found lacking in sixty-one persons who were classified as patients with specific hypersensitivity not related to heredity. The author found that hereditary allergy may be transmitted by the two or either parent in the same ratio of incidence regardless of the sex of the transmissor parent. The first symptoms of allergic disease develop before puberty in persons with bilateral allergy from both parents and after puberty in those with unilateral allergy from either parent, as well as in those with allergy from specific hypersensitivity not related to heredity. In the group of cases reported by the author genotypic predominated over phenotypic heredity. There was bronchial asthma in 100 cases, migraine in twenty-eight, chronic rhinitis in 180, urticaria in twenty, atopic eczema in thirty-two and allergic disturbances of the digestive tract in twenty cases. Evidence of hereditary transmission of an organ of shock was found in none of the cases. Some persons with a history of bilateral or unilateral allergy in the ancestry had prepuberal allergic children. Allergy in these cases followed the same behavior as that of the condition in adults. None of the persons with specific hypersensitivity not related to heredity had children with allergy. The children in this special group were young and far from the prepuberal age.

Sovetskaya Meditsina, Moscow

Pp. 1-48 (No. 11) 1940. **Partial Index**

Oxygen Therapy in Tuberculous and Nontuberculous Pulmonary Disease. V. L. Eynis.—p. 3.
So-Called Idiopathic Pleuritis. V. A. Ravich-Tscherbo.—p. 6.
Newer Therapeutic Methods in Tuberculosis of Upper Respiratory Tract and Mouth. A. N. Voznesenskiy.—p. 10.
Value of Tuberculin Tests in Children. V. D. Markuzon.—p. 13.
Mediastinal Emphysema as Complication of Traumatic Pneumothorax. A. K. Kox.—p. 14.
Active Forms of Tuberculosis. I. I. Ludvinovskiy.—p. 16.
The Jacobaeus Operation in Treatment of Pulmonary Tuberculosis. P. N. Altshuler.—p. 18.
*Treatment of Pulmonary Abscess with Alcohol Enemas. S. I. Mazel.—p. 12.

Alcohol Enemas for Pulmonary Abscess.—The good results obtained in the treatment of acute and subacute pulmonary abscesses with intravenous injections of from 20 to 30 cc. of a 10 per cent solution of alcohol in physiologic solution of sodium chloride suggested to Mazel the rationale of administering it by the rectal route. He believed that the alcohol would be absorbed by the inferior hemorrhoidal vein and thus gain direct access to the pulmonary circulation without passing through the liver. The alcohol exerts a bactericidal effect on the early suppurative focus in the lung, stimulates the reticuloendothelial tissue to the formation of antibodies and assists in obliteration of the formed cavity. The method consisted of a daily preliminary cleansing enema followed in from two to three hours by introduction into the rectum of from 60 to 75 cc. of 10 per cent alcohol in physiologic solution of sodium chloride. The average duration of treatment was from thirty to thirty-five days. After some twenty enemas the temperature, as a rule, fell, the sputum diminished in amount and lost its offensive odor, elastic fibers were no longer present and the general state improved. With further therapy, infiltration and cavities disappeared in roentgenograms. The author reports the results in twenty-nine cases treated since 1937. The duration of the process in twenty-five was from two weeks to five months, and in four from eight to twelve months. Ten patients were cured, eleven much improved, four improved, in two no results were obtained and two died. The author concludes that the rectal method is as effective as the intravenous. The method is most effective in the stage of suppurative infiltration before the formation of a cavity. It is effective in the acute and subacute stage but is of no value in the chronic stage.

Nordisk Medicin, Gothenburg

6:1119-1170 (June 29) 1940

Hospitalstidende

*New Electro-Encephalographic Rhythm in Epilepsy. T. Dalsgaard-Nielsen.—p. 1119.
*Investigations on Vegetative Function in Posttraumatic Dystrophia of Extremities. H. Haldbo.—p. 1124.
Case of Obturation of Mesenterial Blood Vessel. A. Birch-Jensen.—p. 1128.

Electro-Encephalographic Rhythm in Epilepsy.—Dalsgaard-Nielsen reports three cases of symptomatic epilepsy with a peculiar "1 Hertz rhythm" not previously described, which is characterized by (1) regularity, (2) low frequency: "1 Hertz rhythm," (3) low potential, about like that of a normal fronto-occipital Berger rhythm, (4) typical form, with even slow rise and abrupt fall and (5) derivation from a single focus. In the first case there was evidence of cerebral atrophy at the site of the lead, but the history did not suggest traumatic origin. In the second a traumatic etiology seemed possible and there were clinical signs of pathologic changes in the brain at the site of the lead. In the last case, with certain traumatic origin, ventriculography and operation confirmed the presence of a traumatic brain process at the site of the derivation. The author gives warning that there may be sources of error, and furthermore that this rhythm may originate as a pulsation phenomenon, and says that evaluation of the nature and diagnostic importance of the "1 Hertz rhythm" must await the results derived from further examinations.

Vegetative Function in Posttraumatic Dystrophia of Extremities.—Haldbo's examinations in about fifty cases of posttraumatic dystrophy of the extremities, recent distortions and contusions, also some inflammations, showed vasomotor disturbances and disturbances in the secretion of sweat in all cases. He states that as a rule the disturbances disappeared in from two weeks to two months but that they persisted in cases in which halisteresis, edema and cutaneous changes occurred, and anhidrotic parts may extend and gradually occupy an entire extremity. He stresses the practical value of the perspiration test in the surgical clinic as a simple method which allows vegetative disturbances to be followed and timely treatment to be instituted.

Hygiea

*Sulcus Superior Tumors. C. G. Ahlström.—p. 1129.
Disturbances in Albumin Content of Blood. H. Malmros.—p. 1134.
Clinical Value of Galactose Test in Hepatic Disorders. T. Hafström.—p. 1137.

Superior Sulcus Tumors.—Ahlström's first patient, a man aged 36 with increasing radiating pain in the upper thorax for about half a year, was shown by x-ray examination to have a shadow in the apex of the right thoracic cavity, together with partial destruction of the second and third ribs and corresponding processes on the right side. Shortly before death complete paralysis of the lower extremities occurred. Necropsy disclosed a tumor belonging to the chest wall, with subapical localization and only slight marginal infiltration of the lung, destruction of the posterior parts of the second, third and fourth ribs and invasion of the spinal column and compression of the spinal cord. Microscopically the tumor was an endothelioma of the pleura. The second patient, a woman aged 60 with increasing pain and numbness in the left arm for several months, had an apical shadow in the roentgenogram extending to the left hilar region, with atrophy and destruction of the upper ribs on the left side. Necropsy showed a scirrhous tumor, corresponding in structure to that in the first case, in the left thoracic inlet, extensive infiltration of the surrounding tissue, destruction of the upper ribs and dislocation of the apex of the left lung by the tumor, which was intimately attached to the pleura and had only slightly invaded the apex. The author says that the term "sulcus superior tumors" is a collective designation for neoplasms which occur in a certain area of the thoracic inlet and that in practice two kinds of these tumors are to be reckoned with, namely apical lung tumors, which make up the majority of sulcus superior tumors, and tumors of the cupola, which are mainly endotheliomas of the pleura.

THE STUDENT SECTION

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At the Dawn of Modern Youth in Medicine

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LOS ANGELES

The recent graduate in medicine has arrived at an important period in his career without much thought perhaps of how so many apparent obstacles to his progress could have been devised, and why the exacting program in which he has been engaged should be necessary. On reflection, however, it is obvious that obstacles have not been hastily erected nor has the educational program which he has completed been other than constructively arranged. In the evolution of medical education this has occurred in an orderly fashion.

Medical education in this country began in 1765 with the organization of the College of the Philadelphia Department of Medicine, which in 1791 became the University of Pennsylvania Department of Medicine and in 1909 assumed its present title of the University of Pennsylvania School of Medicine. In 1768 this school granted the first medical diploma issued in America. Since the beginning of medical education in America, about 460 medical schools have been chartered in this country and Canada; today there are only eighty-seven approved medical schools in the United States and Canada. In other words, in 140 years about 370 medical schools have come and gone, for there were but five schools in 1800. Medical education in the United States today is regulated by rules and specifications of the American Medical Association, together with those of the Association of American Medical Colleges and by the requirements of the various states for licensure to practice.

In order that one may understand the reason for rules and definite regulations in medical education, it may be stated that the nineteenth century witnessed the organization of many schools for instruction in medicine which were frank commercial enterprises in design and purpose. The general level of practice of the recipients of certification in medicine by many of these schools was low and the tendency was downward. Early in the last century less than 10 per cent of the physicians in this country were graduates of medical schools and more than 80 per cent had not attended lectures in a school of medicine. The need for improvement in methods and the elevation of medical education was apparent as early as 1827. In that year delegates from the medical schools and various societies convened and formulated certain recommendations regarding the length of the medical course, and they suggested that Latin and natural philosophy be required preliminary to the study of medicine. The first national medical convention in the United States was held in 1846 for the purpose of advancing the standards of medical education. At the convention the following year the name of the American Medical Association was adopted.

Even though many other agencies have been cooperative and influential in the advancement of medical education, it has been the object of the American Medical Association throughout the years to promote the science and art of medicine as well as the betterment of the public health, and it has pursued with diligence the self-imposed task of elevating medical education. The effectiveness of rules and specifications for medical education as they have been developed and amplified from time to time may be attested by the failure of so many schools to meet the standards for approval. Consequently such schools soon ceased to exist. It is of interest that today relatively few schools approved by the American Medical Association retain their approval through fulfilment of only the minimum requirements. As a matter of fact, most of the approved medical schools of today are strong medical departments of universities with high educational standards.

As medical education has improved during the years, so has the standard of education preliminary to the study of medicine been elevated. In the educational number of THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION dated Aug. 26, 1939, it may be noted that a baccalaureate degree is required preliminary to admission to five medical schools in the United

Read before the annual meeting of the staff of the Alameda County Hospital, Oakland, Calif., June 6, 1940, on the occasion of presenting certificates to interns and residents of the hospital.

States, that 60 per cent of the medical schools require three years of college work and that only eleven medical schools accept the minimum requirement of two years of preliminary education which is acceptable to the Council. That the standards of preliminary education have been elevated materially is indicated by data from the Council on Medical Education and Hospitals of the American Medical Association, which discloses the interesting fact that in 1910 only 15.3 per cent of the graduates of medical schools in the United States held baccalaureate degrees whereas, in 1932, 71.4 per cent of the graduates held the degree of either A.B. or B.S. A decline to 66.5 per cent of graduates from the seventy-seven approved medical schools in the United States in possession of a baccalaureate degree has occurred since July 1, 1938.

THE PHYSICIAN AN EDUCATED PERSON

I speak of these matters for the purpose of emphasizing that men and women of medicine today are educated persons. They are educated not only in medicine but in the arts and sciences as well. This is in nowise intended as disparaging to those who have preceded us, for it was not their privilege to enjoy and profit from the great educational facilities of today. The stature of many of those of the past was such that they attained memorable and undying distinction in their achievements without the insignia of one of letters, and unlimited tribute is due those of that earlier period who through their earnestness, integrity and splendid personal characteristics were able to maintain the profession on so high a plane with a foundation so unstable, and to hand down to those who followed a legacy to which they contributed so much more than they had received.

Medicine has advanced so rapidly during the past twenty-five years or thereabouts that the curriculum of the medical school has by virtue of necessity undergone great change. Some years ago an opportunity was provided to obtain under supervision at least some practical experience during the clinical years. The crowding of the curriculum with the requirements of the medical education of today has largely eliminated that opportunity. Practical experience can be obtained now only through internship, residency and what constitutes organized postgraduate training. The University of Minnesota was the first to make practical rectification of this situation in medical education and since 1915 it has exacted a year's internship requisite to the degree of Doctor of Medicine. Thirteen medical schools in the United States and Canada now require the internship for the degree of Doctor of Medicine. One of these, Duke University, requires two years' internship, even though the M.D. degree is granted after completion of the senior year. Twenty-two states, the District of Columbia, Alaska and Puerto Rico require hospital internship of all applicants for licensure.

It may seem to those who are unfamiliar with the past, and to those who are not cognizant and aware of the magnitude of the science of medicine, that the program of education and training imposed on the aspirant to fellowship in the medical profession is unduly burdensome in educational attainments required, in time consumed and in energy expended. It should be stated that the magnitude of the science of medicine is unlimited, in medicine one consumes all time, medicine commands one's entire effort and energy, and educational attainments of the highest order are essential for even a modest comprehension of all that medicine involves. Medicine is a chosen profession but a profession which accepts only those who are physically, mentally and morally qualified not only to endure its prerequisites but to challenge and engage the problems and responsibilities of its sphere. Medicine likewise rejects those who have ambition without cause.

The recent graduate in medicine has had but one educational highway along which he could proceed with others to attain his present station. There now lies before him a maze of routes diverging from that which he has just traversed and undoubtedly he has experienced some bewilderment in the selection of his future course and has wondered what his ultimate destination in medicine may be. It is during one's youth in medicine that one's individual traits, inherent aptitude, talents, capabilities, natural tendencies and physical, mental and moral characteristics as they have been influenced by what has preceded will take form and mold one as a distinctive individual in medicine. One will proceed in medicine as one has been molded. Fortunate indeed are those who through predilection have chosen a future course, leaving them unencumbered by indecision to pursue their objectives. Indecision and uncertainty on the part of the recent graduate should not be disconcerting, and that an open highway to his own desirable objective, equipped with a conveyance assuring him of easy and comfortable passage, is not immediately visible and available to him should not serve to discourage. Instead, one should be mindful that Pasteur, Lister and others were among the many whose achievements have been notable, epoch making, revolutionary and not infrequently subjected to bitter challenge and that they hewed and hacked their own road through virgin forest. One may say that this was long ago and can no longer occur. The reply is that new roads and by-ways are being driven into the unknown of medicine today and that the achievements in the advancement of medical science of today will be ranked with

those of the past by the future historian. A multitude of opportunities continue to exist in medicine for those of discernment, initiative and the will to do.

POSTGRADUATE TRAINING AND EXPERIENCE

The graduate in medicine today is a sound product of modern education and is better prepared fundamentally in all phases of medicine than were his predecessors to engage the problems and responsibilities; yet, inconsistent as it may seem, the door to the field of active practice has not been flung wide but stands ajar to those who may with courage but without wisdom venture forth. This reflects not on the educational program that the graduate has just completed but is due to the demands of modern practice. Pasteur said "Chance favors the prepared mind." Another has said "The prepared mind is a mind stored with the history and fruits of human experience. It is a mind which has been called upon in the course of its education to deal with problems, now of one kind, now of another. It is a mind fitted to enjoy and to be guided by the spiritual experiences of the human race." An intellectual preparation of the mind occurs while one is engaged and occupied in a formal educational program or curriculum. Maturity of mind occurs only through experience in the subsequent formal and informal activities of human endeavor. Herein lies the necessity for and the value of adequate postgraduate training and experience. The question of what constitutes adequate postgraduate training and experience is immediately in order, and it cannot be answered in a dogmatic fashion or without deliberation.

A period of more or less formal and organized study in hospitals and clinics immediately following the completion of the medical curriculum is the order of the day. The length of time which can be spent in such postgraduate study and supervised experience varies from a minimum of one year's internship to a carefully organized progressive program of approximately seven years in a few institutions, wherein unusual facilities for such training exist or have been organized, with from three to five years constituting the period in many institutions. As to just what type of postgraduate training one may engage in following the internship and where the desired training may be obtained constitutes a problem the solution of which is often extremely difficult. Irrespective of what branch of medicine one wishes to make one's life work, it is generally agreed that the broad foundation gained from a rotating internship provides the most stable footing from which one may progress. One's own inherent talent in a certain direction is perhaps the most important influence. One should aspire to employ one's time and energies in the direction of that phase of medicine to which one has been attracted and in which one has demonstrated to oneself and to others that one possesses talent. There are many in medicine who have not chosen their sphere wisely, who through inherent deficiencies requisite to the pursuit of certain branches of medicine are totally unfit, but who in another field of medicine might proceed with credit and even bring luster to their names and to the medical profession as well.

Fortunate indeed is he who either during his student days or while engaged in his internship has recognized that within himself there are certain attributes which qualifiy him peculiarly and particularly in a special branch of medicine. And fortunate indeed is he who during this period has come under the influence of an inspirational preceptor who has recognized a dormant or latent talent and has sparked the mechanism which propels the youth to otherwise unattainable heights in medicine. The necessity for the firing of ambition in medicine is great, and that fire must continue to burn in order that one may progress. This is spoken without reference to any particular branch of medicine. Fire is as essential to general practice as it is to any of the specialties. Work is the center of the circumference of one's life in medicine, and only through the ambitious pursuit of one's work can one continue to enjoy the routine tasks and smile at disappointment. It should be emphasized that, irrespective of the branch of medicine that one wishes to pursue, there are many routine tasks and as many disappointments. It is essential that one develop a philosophy good for all weathers.

GENERAL PRACTICE AND THE SPECIALTIES

Those who choose to engage in general practice must of necessity sacrifice depth of knowledge in favor of breadth. Herrick has said "To the brilliant mind of half a century ago a working knowledge of all the departments of medicine was attainable; today such a progeny is impossible." The field of general practice is broad, but through specialization depth of knowledge has been made available in accordance with modern practice. Specialization in the various fields of medicine provides for proficiency when proper correlation of the specialties and of the specialist exists but inadequately serves when carried to organs or systems of organs with narrowing of vision and loss of the perspective of the organism as a whole.

Those who have chosen to engage in general practice are legally qualified to do so, and their moral qualifications will exhibit themselves as they refrain from attempting the use of methods and the performance of technical procedures in which they have not been trained. Those who aspire to proficiency in a special field of medicine need not sacrifice breadth of medical

knowledge but must attune themselves to the depths of the special field and to the time and energy requisite to the attainment of recognized proficiency. To speak specifically in medicine it is not enough that one know when and how much insulin shall be administered to the diabetic patient; one must know all that is known about the disease, its allied metabolic disturbances and the basic therapeutic principles. It is not enough that one know that the administration of vitamin K and bile salts serves as a specific in the control of the hemorrhagic tendency in obstructive jaundice and in certain other prothrombin deficiency states. It is not enough that one know much of the present in medicine and little of its past. It is not enough if one does not now know or if one does not learn as one progresses the processes through which medicine had advanced. No cursory survey of a subject or of a field of medicine today qualifies one as outstandingly proficient in that branch. There is no short road or circuitous route by which one can arrive at proficiency in any of the specialties of medicine. This is particularly true of surgery and its allied specialties. It is true that the degree of proficiency attained by those who pursue a prolonged period of formal training in surgery is a variable one. Proficiency in surgery depends on many factors. I cannot define them all. The surgeon may become mature but he is never a finished product. To progress he must grow, and to increase his surgical stature requires physical, mental and moral sustenance. Surgery commands certain attributes which fundamentally are inherent, and without these the seeds of training fall on infertile soil. One is not born a surgeon, but a surgeon is born with certain inherent qualities which influence those that may be acquired. Postgraduate training may enable one to execute surgical procedures skilfully and under supervision exhibit a tendency to stay a courageous hand, but something more is essential to the proper direction of the mind and the hand of the surgeon. The moral ingredient of man provides the foundation for the rearing of judgment which must guide the surgeon in the utilization of his knowledge and the application of his skill.

To those who aspire to proficiency in surgery or in one of its allied fields I should like to appraise the depths. As no one untrained can successfully explore the depths of the sea, so can no one venture without adequate postgraduate training, and the resultant armamentarium, into the field of surgery with hope to achieve. To define adequate postgraduate training in surgery is not dogmatically possible. However, certain minimum standards have been erected by the American College of Surgeons and by the various American boards for certification of the specialist by which his status may be recognized. This is all in entire conformity with the ideals of medicine to leave it better than when it was found.

CHALLENGE TO PROGRESS

As one proceeds through life in medicine one will find it of advantage to maintain a progressive spirit, and to progress one cannot with aristocratic detachment go his own way. The fellowship that one can enjoy with his colleagues in medicine provides the stimulation so constantly necessary in an exacting profession. One will find as one proceeds day by day and from one year to another that one's progress is constantly subject to formal, informal, visible and invisible challenge. No two words express so eloquently the significance of that daily challenge in medicine as do those comprising the title of Lloyd Douglas's recent book "Disputed Passage." You at this time have in common with your faculty members and your preceptors only one distinction, possession of the degree of Doctor of Medicine. As to whether you will adorn that distinction depends not only on the height but on the manner of your achievements.

I would repeat that the man of medicine today is an educated man. He is educated not only in medicine but in the arts and sciences as well. It is expected of him, and not unjustly so, that his thoughts, his spoken words and his conduct shall at all times and under all circumstances reflect with honor and distinction on his own inherent capacity, opportunity and privilege to attain the high educational status that qualifies him to receive at the hands of those who are authorized to bestow them the insignia by which he may be recognized as an educated man and a doctor of medicine. The man of medicine who utilizes his premedical education in the arts and sciences not as a springboard to the medical curriculum but as the foundation for the building of a broad culture wherein the spiritual phase of medicine arranges a perspective through which ideals can be appreciated will find happiness and success by his own measure of achievement.

It is my hope as you engage the problems and responsibilities of your chosen profession that you will at all times and under all circumstances perform your professional duties with compassion, unselfishness and honor; that in your work you will always find happiness but will never be entirely content with your progress; that when you have completed your life's work your contributions, humble as they may be, will have served to make the profession of medicine better than one finds it today. It is my wish to leave with you the words of Albert Pike, who said "What we have done for ourselves dies with us, what we have done for others and the world remains and is immortal."

561 Roosevelt Building.

Digests and Reviews

TO THOSE ENTERING THE MEDICAL WARDS

By Dr. A. H. Douthwaite. Slightly abridged from Guy's Hospital Gazette, Oct. 22, 1938.

The physical transition from medical school to the wards is of small moment; it is the complete change in the character of work, the acceptance of actual responsibility for sick people and, more than all, the observance of their mental reactions which mark this as an epoch of considerable significance. Those of you who come to us from other schools may be struck by the absence of formality which exists at Guy's. Though subjected to criticism from some quarters, it is, I believe, a desirable feature inseparably linked with the policy of producing men trained to be practical rather than those nurtured on compulsory lectures now rendered an anachronism by a superfluity of textbooks. Rather do we invite you to accompany your teachers in the wards, see the problems for yourselves, ask questions when you will, and argue if you wish. Perhaps you have had mediocre success in the medical school and this has led you to doubt your ability to clear the last fences. Banish the fear. The best clinicians often emerge from such unpromising beginnings.

The next few years will be hard; the days of long holidays are over, for a fortnight out of an appointment is the maximum which can be taken lest valuable experience be sacrificed. The curtailment of time for relaxation is fortunately well compensated for by an infinite variety of enthralling experience.

As to the planning of your studies, accept the fact that last-minute cramming for final examinations is of no use. The subject is too vast for any than gradual absorption, so it is well to follow some plan from the outset. The preliminary clinical period prepares you thoroughly for the routine examination of patients and thus prevents waste of time when you enter the wards. Beds and their human contents are allotted to you, and therewith your share of responsibility. The taking of the medical history is the most important step toward arriving at diagnosis. This is primarily your job and its value cannot be overemphasized, though too often forgotten in a desire to search for physical signs of disease. The ability to sift the relevant facts from matter which obscures can come only with experience. In the meantime bear in mind the value of facts, as opposed to patients' interpretation of them, and of their presentation in a legible and, where possible, schematic form. When writing a report, do so with the thought that on its accuracy may depend the outcome of valuable research undertaken years later. Whenever possible, examine your patient before he is seen by the registrar and commit yourself to a diagnosis. Progress of the disease, ultimate outcome, treatment given, opinions expressed on diagnosis, should all be entered to make the records of lasting value. Forms are now issued on which you can write down your observations and conclusions, and this should invariably be done. It is the only way to avoid that type of mental dishonesty which leads to brilliant differential diagnoses any one of which can be claimed as a personal success at a later date! This dangerous habit once acquired is difficult to discard. It meets with but scant respect, however, from the relatives of the sick. Mistakes have a high educative value. They snatch one with a jerk from the danger of self complacence.

Probably the best plan of study is to concentrate for the first three months on pathology. This entails, of course, frequent visits to the postmortem room. Given this grounding, symptoms and signs become the natural expression of the disease and their memorizing is unnecessary. Probably the most valuable time of the day for the acquirement of practical knowledge is that which follows the afternoon round. It is then that the house physician performs lumbar punctures, collects blood, taps chests and so on. These procedures should be watched and from time to time you will be given the opportunity of carrying them out yourself. It is now also that special signs referred to in the teaching round can be reexamined and thus fixed in the memory. It should be made a point of pride that within a fortnight you should be able to inspect the optic disks of any patient you may choose. Once the knack has been acquired, and it usually comes quite suddenly after several days of disappointment, it will never be lost. It takes many months to be certain of the normal as opposed to the diseased disk, yet recognition of early change may be of the utmost importance in determining a diagnosis and possibly even in saving a life.

The patients in your beds will confide in you possibly more than in the house officers or staff. To them you are their doctor and from you they will try to get confirmation of their fears in respect of illness, or of suspicions in relation to earlier treatment. An immense amount of mischief is caused by the making of unguarded remarks which can be misconstrued. Their avoidance is doubly difficult in a teaching hospital, where a discussion on the problem is too often carried out within earshot of the patients. We all err unwittingly in this respect, and the

importance of discretion needs reiterating. The fact that a patient can inspect his own report is deplorable and should be remedied.

Attend outpatients when you can. This is the only hospital activity which remotely approaches the conditions which obtain in general practice. The frequent absence of physical signs may be tedious, but precisely for this reason is the experience invaluable in forcing you to rely more and more on history taking. It is an antidote to the poison of mechanized medicine, the virulence of which increases with every new instrumental aid to diagnosis.

Don't live near the hospital until you have to. Knowledge is not in the air; disease is.

Go away for week ends.

Take holidays, abroad if possible, and with anybody who is not a medical student or a doctor.

Be active in the debating society. The ability to stand on one's legs and talk is acquired painfully by many of us. Its value is inestimable.

Insure your life and health, and join a society for protection against possible legal proceedings as soon as you are qualified.

In moments of despondency remember that medicine is the only profession which never provides two days which are alike and in which boredom is a rarity.

THE BROADENING HORIZONS OF MEDICINE

Condensation of an article by Dr. Winfred Overholser, read at the opening session of George Washington University School of Medicine, Washington, D. C., Sept. 25, 1939, and published in Science, Oct 20, 1939.

Many of those present today are taking their first steps along the road which leads to the practice of medicine. The road is difficult. Even those who are present today for the first time have already spent two years or more in college studying premedical subjects. They must spend four years of study in the medical school, after which there will come a period of internship. I am bold enough to question the wisdom of some of the required premedical work. There is a tendency today to require specialism altogether too early and to leave out of the equipment of the medical man what were known in the old days as the humanities. Although medicine has developed almost unbelievably, there are still other things which make life worth living and to which the medical man should not be inattentive. Let us hope that the day is not gone forever when medicine can produce such littérateurs as Oliver Wendell Holmes, S. Weir Mitchell, Sir William Osler and Harvey Cushing. I recommend as a decided contribution to a balanced mind the development of hobbies to which one can occasionally flee from the practice of medicine.

ATTRIBUTES OF A PHYSICIAN

In the midst of a cynical world it is well to reaffirm one's faith in such a thing as altruism, the desire to serve one's fellow men. I may be pardoned a quotation by referring to the tribute paid to the physician by Robert Louis Stevenson. The physician, as a rule, he comments, stands above the common herd, shares as little as any in the defects of a period and most notably exhibits the virtues of the race; he says of the physician: Generosity he has, such as is possible to those who practice an art, never to those who drive a trade; discretion tested by a hundred secrets; tact tried in a thousand embarrassments; and, what are more important, Heraclean cheerfulness and courage. So it is that he brings air and cheer into the sickroom and often enough, though not as often as he wishes, brings healing.

RELATION OF PHYSICIAN TO PATIENT

It is well to give heed to what is meant by a learned profession as distinguished from a trade or business. The professional man is guided by the ideals of his profession, rules of conduct which have been handed down and which are embodied for the medical man in the Hippocratic Oath. He is primarily a learned man who depends on his knowledge as his stock in trade. He has specialized knowledge over and above that of the common man in relation to some particular topic. Perhaps the thing that distinguishes him more than anything else is the peculiarly personal relation to the client or patient which he enjoys, a confidential relationship, a situation in which he is adviser, guide and friend, a situation in which his interest does not cease when the particular transaction is concluded. He is an individualist, one who functions far more efficiently without regimentation or coercion, but rather requires the opportunity to utilize freely his own initiative and judgment within the limits of his professional code of ethics.

He has an interest in the results of this relationship in which he is called to advise, which is over and above the cash recompense which he receives; in fact, in the practice of medicine it is all too often the case that no monetary recompense is received at all, and more frequently the recompense is wholly inadequate to the value of the services rendered. The physician does not consider that he is receiving a *quid pro quo* when he is paid by his patient. He is entitled to a living, but more than that he takes a satisfaction in seeing that the results of his advice have brought aid and comfort to the person who sought it.

Another feature is the disregard of fixed hours, the readiness to be of service whenever called on. He does not count on regular hours. He realizes when he takes up the study of medicine that his sleep will often he interrupted,

that his time will not really be his own, and he rejoices to feel that he may be called on when others are in need regardless of his own comfort. One other point of distinction is the principle as laid down in the Hippocratic Oath that he will teach this art to others, if they wish to learn it, "without fee or stipulation." Such are some of the distinctions which set off the learned professions, and particularly the profession of medicine, from business.

WILLIAM ALANSON WHITE

We have been deeply touched this morning by the presentation of the oil portrait of Dr. William Alanson White, the gift of the faculty to the school. I look on Dr. White as the ideal medical man. He was a student; he always wished to learn. He was a teacher, always happy in imparting his knowledge to others, a gift which he had in rare measure. He was deeply interested in the patient and desired first to understand the nature of the disorder. Whether or not he brought healing, he always brought comfort. At the same time he remained a human being, a man in close touch with his fellow men, a man of wide and scholarly interests.

A CENTURY OF PROGRESS

The significant advances in medicine in the last century are too many to be enumerated here. Consider the advances of bacteriology, the significant work of Morton, Lister and Pasteur, and more recently of Banting and his development of insulin, the work of Theobald Smith and McKinley in bacteriology, the work of Folin in chemistry and of Cannon in physiology, the development of the knowledge of the vitamins and of the endocrine glands, and of surgery. Perhaps even more important is the aspect of preventive medicine for which Walter Reed did so much. Today diphtheria, typhoid and many other diseases are virtually unknown. New horizons are being discovered daily in the field of allergy.

Let us not be deceived into thinking that human improvement is nearly ended. There is ample room for improvement. Much more is to be learned concerning the possibilities in the field of heredity and constitution, and in bacteriology with particular reference to the virus diseases and the development of biologic tests. Chemotherapy is only beginning. Surgery is on the threshold of new developments. The newer anesthetics in the field of obstetrics have revolutionized the practice of that specialty within the past few years. There is one field, however, on which medicine has hardly yet begun—medicine is just discovering man! So much in the past has been devoted to the parts of man, to his various organs, systems and specific functions that too little has been thought about man himself, the social animal whose principal significance is his relations with other men. Dr. William A. White probably did more than any other medical man in this country to emphasize the importance of the individual, the "organism-as-a-whole," as he called it, a something which is greater and more important than the sum of all its parts, and indeed something different from the sum of its parts. He emphasized the fact, now just beginning to be recognized generally, that the influences which impinge on one from the outside, as well as the conflicts which arise from one's unconscious, have much to do with the physical functioning of the organism. So much attention was focused on the gastrointestinal and circulatory tract that it was forgotten that they were parts of an individual who was perhaps expressing in this particular way and by these particular symptoms his emotional conflicts. The field of psychosomatic medicine is in its infancy. It is encouraging to note recently in THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION moderately frequent references to the psychic factors in disease. A tremendous expansion in the psychiatric approach to medicine may be looked for, and in this field we shall be constantly indebted to the contributions of Dr. White.

Even though the world is troubled, we may look for peace and satisfaction in the field of medicine, which is only at the beginning of possibilities of service and benefit to mankind. That medicine will continue as a profession in the hands of men possessed of individual initiative and of professional ideals we need have no doubt.

MEDICAL RESEARCH: THE STORY OF SULFANILAMIDE

Abstract of address by Dr. E. K. Marshall Jr. published in the North Carolina Medical Journal, March 1940.

A school of medicine has primarily two objectives: the training of future physicians and the advancement of knowledge by medical research. For the attainment of the first, the second, properly pursued, is necessary. Organized medical research, at least in the so-called preclinical subjects, is a recent innovation. With the partial exception of the anatomic laboratory, laboratories in medical schools for the training of students and for research are largely creations of the last three quarters of a century. The first pathologic laboratory was founded by Virchow in Berlin in 1856; physiologic chemistry as a separate discipline split off from physiology quite late, and Hoppe-Seyler headed the first independent laboratory devoted to this subject at Strasbourg in 1872; pharmacology as the experimental science we now know began when Buchheim established its first laboratory in his private house at Dorpat in 1849. Coincident with the growth of organ-

ized laboratories for medical research the whole face of medicine has changed, and it is probably no exaggeration to say that a greater advance has been made in medicine in this seventy-five year period of laboratories than in all previous medical history. The lot of the diseased person today is immeasurably improved over what it was a hundred years ago. This improvement is the result of the labors of thousands of unknown medical research workers before whom stands the challenge of the prevention, alleviation and cure of human diseases. The lessons of science show, however, that the investigator having a definite practical goal in view frequently defeats his own ends by his impatience of any but the paths that seem direct and obvious. Important discoveries come generally from the work of those who seek knowledge for its own sake. The man into whose lap the fruit of discovery falls has builded on countless pieces of research and the long labors of a host of other investigators. No one can tell when knowledge acquired by an investigator satisfying his intellectual curiosity in a field of medical research apparently quite remote from practical things may be vital to the health of mankind.

Permit me to illustrate. You all know that in the last three years sulfanilamide has been used for the treatment of infections. Its introduction into medicine is to be ranked with the two great therapeutic discoveries of all medicine—the discovery of anesthesia and that of aseptic surgery. The story starts in 1904, when Ehrlich and Shiga first showed that a fatal experimental infection of mice caused by a trypanosome could be cured by a single injection of a relatively harmless red dye. Six years later Ehrlich announced the discovery of a cure for syphilis. Despite advances since Ehrlich's time in the chemotherapy of protozoan infections, nothing of practical importance was developed in the chemotherapy of bacterial infections until the sulfonamide group was introduced. In 1911 Morgenroth and Levy found that a chemical related to quinine—ethylhydrocupreine—would cure pneumococcic septicemia in mice. However, when this remedy was tried in pneumonia in man it was found too toxic to be given in sufficient dosage for effective therapy. In 1908 sulfanilamide was prepared by a chemist, Gelmo, working at the Royal Technical Hochschule of Vienna, apparently solely to satisfy his curiosity. A year later chemists at Elberfeld, Germany, prepared azo dyes with sulfonamide groups and found that they were distinguished by greater fastness to washing and milling than the corresponding sulfonamide-free products. No attempt was made at this time to apply these compounds to the control of bacterial infections. Domagk announced in 1935 that an azo dye containing the sulfonamide group prepared by Mietsch and Klarer would cure an otherwise fatal streptococcic infection in mice. This compound, azosulfamide, was originally called prontosil. Clinical reports attesting the efficacy of azosulfamide in patients with streptococcic infections appeared shortly before and at the same time as Domagk's announcement of his discovery. Workers at the Pasteur Institute late in 1935 suggested that azosulfamide was broken down in the body to form sulfanilamide, which was found to be as effective as azosulfamide. This important observation demonstrated that a relatively simple organic compound was effective as a chemotherapeutic agent in streptococcic infections. English investigators in 1936 confirmed, as Long and Bliss did later in America, the fact that both azosulfamide and sulfanilamide would cure an otherwise fatal streptococcic infection in mice. With the publication of a paper in 1936 by Colebrook and Kenny of Queen Charlotte Square Hospital in London on the results in child-bed fever, much interest was awakened in these new drugs.

Sulfanilamide has been proved to be a specific in certain infectious diseases in human beings. It produces however at the same time in some cases toxic effects, some of which may endanger the patient's life. Numerous drugs allied to sulfanilamide have been tried. Sulfapyridine has proved about as effective in pneumococcic pneumonia and meningitis as is sulfanilamide in hemolytic streptococcus infections. The question of the mechanism of action of these new drugs is important. If it could be solved, the search for still better drugs for treating infections would be put on a firm scientific basis. Research is needed to complete the picture.

THE PREDICTIVE VALUE OF THE MEDICAL APTITUDE TEST

A study was made at Vanderbilt University School of Medicine, Nashville, Tenn., of 191 students who had taken the medical aptitude test and also of about fifty-five students who were accepted without having taken the aptitude test. The records of the students studied covered in all a period of nine years. The object was to compare the merits of the aptitude test and the premedical grades in predicting the degree of success of medical students; also to determine the degree of correlation between aptitude test scores of premedical students and their success in the four years of medical school work. The data are presented in charts published by Beverly Douglas,[1] the assistant dean. Obviously, if the aptitude test can help to predict the success of a student in the freshman year it is valuable. The aptitude test has never been required at Vanderbilt; nevertheless it has always been advised and in some cases insisted

1. Douglas, Beverly: A Study of the Predictive Value of the Medical Aptitude Test at Vanderbilt School of Medicine, J. A. Am. M. Coll. **13**: 380 (Nov.) 1938.

on. It should not be regarded, however, as the sole criterion by which a student should be judged. In summarizing the data presented, the author says that the predicted value of premedical grades, both scientific and general, is fair in the case of certain classes and poor in certain others. In none was it significant enough to be used as a sole and presumptive index of a student's likelihood to succeed in medical school. These studies show that premedical grades were not as good a criterion as the aptitude test in predicting the success of students at Vanderbilt; nevertheless they were considered valuable and are expected to become more so as certain colleges improve their courses and grading systems. When the personal rating forms, the premedical grades and the aptitude test scores are considered together they give a more accurate prediction of a student's worth than when any one or any two criteria are considered in choosing between so many applicants when there are so few places available (each year at Vanderbilt there are more than 700 applicants for the fifty available places), every criterion which has any value should be taken into account. Certain students will nevertheless later defeat all predictions. The author cites a case. Dr. William Sydney Thayer was expelled from Harvard because of a boyish prank and probably would not have been allowed to enter medical school had it not been for the sympathetic efforts of an old English clergyman. The author hopes that, in the endeavor to choose the right applicants for medical training, no Parés and no Oslers will be excluded.

Comments

The number of crippled children registered in forty-five of the states of this country at the beginning of 1940 was 188,579, of which 29,849 were registered in New York, 26,953 in Illinois, 15,343 in North Carolina, 11,304 in Michigan, 10,174 in Texas and 10,049 in New Jersey. Poliomyelitis caused crippling in 36,271 of these persons under 21 years of age, cerebral palsy in 19,172, paralysis due to birth injury exclusive of cerebral palsy in 4,532, tuberculosis of bones and joints in 7,196, osteomyelitis in 11,112 and burns in 4,161.

Hugo Iltis, the biographer of Gregor Mendel, is now professor of physiology at Mary Washington College, Fredericksburg, Va. Dr. Iltis was born in Mendel's home town, Brno, Czechoslovakia, and besides writing the only biography of Mendel he built up the only Mendel museum in the world. A distinguished committee with Henry A. Wallace, Secretary of Agriculture, honorary chairman, has become interested in establishing a Mendel museum in the United States. Consideration is being given to an appeal to the public for subscriptions to make the Mendel exhibit available to the public. Dr. Iltis collected from the Augustinian monastery at Brno, where Mendel did his work, the original manuscripts of Mendel's papers on atomic heredity, Mendel's diary, letters to and from his contemporaries and Mendel's notes on genetics, bees, meteorology and horticulture.

The number of applicants for admission to the freshman class of seventy-seven medical colleges in the United States in 1939 was 11,800, of whom 6,211, or 52.7 per cent, were accepted and 5,589 were rejected. The 11,800 applicants made 34,871 applications, one applicant having made as many as forty applications, none of which were accepted. The number of applicants dropped in 1939 below 12,000 for the first time in eight years. The percentage of applicants accepted has dropped from 62.1 in 1933 to 52.7 in 1939.—*Fred C. Zapffe*, Chicago, Secretary, Association of American Medical Colleges.

DO YOU KNOW WHAT PHYSICIAN—

1. Sent Paul Revere on his famous ride to Concord and Lexington and later was killed at the Battle of Bunker Hill?

2. Invented (1861) the revolving machine gun, which bears his name?

3. Was Premier of France during the first World War?

4. Wrote "In Flanders' Fields"?

5. Was the first to evolve a system of shorthand writing?

6. Wrote the Adventures of Sherlock Holmes?

7. Was the first president of the Chinese Republic?

The answers are on page 1150.

Medical College News

Medical schools, hospitals and individuals will confer a favor by sending to these headquarters original contributions, reviews and news items for consideration for publication in the Student Section.

The Gold-Headed Cane

Leslie L. Bennett, '40, University of California Medical School, San Francisco, was awarded the gold-headed cane which is given each year to the student adjudged most likely to become eminently successful in his profession. Archer Jule Sokol, '41, and David E. Price, '40, received honorable mention in the cane competition and were awarded copies of a book describing the ancient cane ceremony. The university ceremony is adapted from an old English tradition in which a single gold-headed cane was handed down through several generations of eminent British physicians.

First Appointee to the Luckhardt Fellowship

At the annual banquet of alumni of Rush Medical College in Chicago, June 6, Prof. Anton J. Carlson, toastmaster, announced that contributions to the Arno B. Luckhardt fellowship were now sufficient to provide an income of about $1,000 a year. The first appointee to the scholarship is Dr. Alexander Rush, the great-great-grandson of Dr. Benjamin Rush, signer of the Declaration of Independence, in whose honor Rush Medical College was named.

Commencement at Jefferson

The graduating class of 125 members at Jefferson Medical College of Philadelphia at the 115th commencement, June 7, brought the total number of graduates of this school to 16,694. Thirty-one members of the graduating class were commissioned first lieutenants in the medical section of the Officers' Reserve Corps, the commissions being presented by Lieut. Col. John F. Corby, M. C., U. S. Army. The graduates originated in twenty different states, Hawaii and Puerto Rico. The class presented to the college a portrait of the dean, Dr. Henry K. Mohler. The valedictory address was delivered by William L. Phelps, Ph.D., Yale University, New Haven, Conn., whose subject was "The Art of Living."

Harvard's National Scholarships

The recipients of national scholarships for admission this fall to Harvard Medical School, Boston, were announced June 9. They are James S. Clarke, LaGrange, Ill., awarded the Daniel Fiske Jones National Scholarship; Martin E. Flipse, Douglaston, L. I., N. Y., the Edward S. Harkness National Scholarship, and Windsor C. Schmidt, Rye, N. Y., the Harvard Medical School National Scholarship. This is the fourth year of Harvard Medical School's scholarship plan.

Additional medical school scholarships totaling $1,300 were awarded to James P. Dixon Jr., Yellow Springs, Ohio (Matthew and Mary E. Bartlett Scholarship); Lytt I. Gardner, Reidsville, N. C. (Abraham A. Watson Scholarship), and Frank E. Trobaugh Jr., West Frankfort, Ill. (Isaac Sweetzer Scholarship).

Louisiana's Graduating Class

Sixty-nine students of Louisiana State University School of Medicine, New Orleans, received the M.D. degree at the commencement in Baton Rouge, June 3, and forty-five of them were from the state of Louisiana. The five students who made the highest averages were, in order of standing, James T. Nix Jr., New Orleans; Harold B. Levy, Shreveport; William Rigsby Hargrove III, Oakdale; Milton Flocks, Baltimore, and Marion J. LeDoux, New Orleans.

Colorado Students Organize Seminars

The junior students at the University of Colorado School of Medicine, Denver, recently organized seminars in surgery, medicine, obstetrics and psychiatry which will meet monthly at the home of a sponsoring faculty member. The groups are limited to fifteen students, two or more of whom read papers at each meeting. The seminar in medicine, sponsored by Dr. John G. Ryan, is devoting its first two meetings this year to kidney diseases; the seminar in surgery, sponsored by Drs. Frederick Harper, Casper Hegner and Leonard Freeman Jr., is to devote this year's seminars to surgery of the gastrointestinal tract. The seminar in psychiatry, sponsored by Dr. Edward Billings, will devote all of this year's meetings to psychosomatic problems, especially those referable to the heart and gastrointestinal tract. The organization of the seminar in obstetrics has not been entirely completed.

California's Osler Society

Twelve members of the sophomore class of the University of California Medical School, San Francisco, met recently to form an Osler society. The organization will follow the tradition of the Osler Society at McGill University Faculty of Medicine, Quebec, which society has served as a model for many similar societies in this country and abroad. The California society will meet four times a year, at which time papers will be read by members on subjects related to medical history and to the life of Sir William Osler.

Award to Oklahoma Student

The University of Oklahoma has announced three $50 scholarships to be awarded annually to a member of the senior class of the schools of medicine, law and engineering whose grades are in the upper 25 per cent of the class, who has earned by personal service at least 50 per cent of the cost of his college education to date and who has developed a sense of self reliance and honesty of purpose. Mr. James Lowden Dennis, '40, was this year's recipient from the school of medicine.

Western Reserve Increases Tuition Fees

Western Reserve University announces that the basic fee in its medical school will be increased from $400 to $500 for all classes beginning with the academic year of 1941 to 1942. The announcement is made a full year in advance to give students the opportunity to adjust themselves to the situation. The increase is necessary to meet in part the diminished returns of endowments. Incidental fees remain essentially at the present level.

Louisiana Discontinues the Tiger

The *Tiger*, which has been the weekly official organ of the students of the Louisiana State University School of Medicine, New Orleans, since 1932, has been discontinued and a monthly publication to be known as the *Journal of the School of Medicine of Louisiana State University* will be substituted for it. The editor of the new publication is Thomas R. Wilson, '41; Laurence B. Weiss, former managing editor of the *Tiger*, will serve as co-editor. Drs. Edward L. Burns, Hugh C. Ilgenfritz and George W. McCoy will serve as an advisory board from the faculty.

Premedical Symposium at Duke

Duke University School of Medicine, Durham, N. C., presented a symposium on premedical education, April 26, under the auspices of the premedical society of the university. Dr. Frederic M. Hanes was chairman of a clinic for premedical students held in the amphitheater of Duke Hospital, at which several members of the faculty made brief remarks. The clinic was followed by an inspection of the hospital and of the medical school by the premedical students, and at 4 p. m. the public also was invited to hear an address on "Educational Backgrounds for the Study of Medicine" by the dean of the University of North Carolina School of Medicine, Dr. William deB. MacNider. In the evening the public was also invited to a round table discussion on premedical education, at which Dr. Wilburt C. Davison, the dean of Duke University School of Medicine, was chairman. Question boxes were placed at the various meetings and any one present could thus bring up a topic for the round table discussion. The participants in the round table discussion included Dr. MacNider, Dr. Thomas T. Jones, Dr. Charles E. Gardner, several members of the premedical faculty, William M. Eagles, president of the premedical society, and Frank Bone and Arthur A. Morris Jr., premedical students, graduates of the university in 1940. The president of the premedical society was chairman of one of the afternoon meetings.

Wayne Withdraws from Association of Students

The Wayne University College of Medicine chapter of the Association of Medical Students announced, June 5, the severance of its affiliation with that association. This was felt necessary owing to extramedical activities of the Association of Medical Students which the Wayne chapter felt inconsistent with its own policies and those of the Wayne University College of Medicine, Detroit.

Prize Papers at Indiana

Three courses given at the Indiana University School of Medicine, Indianapolis, require term papers: bacteriology, surgical pathology and history of medicine. Recently, however, the heads of all departments were asked for outstanding case reports, essays submitted by students or statistical studies, and 325 papers were received, of which the following were selected for prizes:

JUNIORS

Miss Antha A. Hamilton, First prize—"The Treatment of Hemophilia"	$20.00
Harry D. Schell—"Capillary Permeability"	15.00
Julius T. Steffen—"Physiology of Lymph Production and Flow"	15.00
Joseph R. Eastman Jr.—"Arteriovenous Aneurysms"	15.00
Richard K. Parrish—"Local Tissue Immunity"	15.00
Philip W. Hedrick—"Air Borne Infections in the Surgery"	15.00
Ottis N. Olvey—"Effects of Obstetrical Anesthesias and Analgesias on the Newborn"	15.00

SOPHOMORES

Thomas L. Ditmer—"Typhoid Carriers"	$15.00
Guy B. Ingwell—"Rocky Mountain Spotted Fever with Special Reference to Indiana"	15.00
Everett L. Kalb—"Use of Heparin and Sulfapyridine in the Treatment of Subacute Bacterial Endocarditis"	15.00
Helen M. Sisson—"Impetigo Contagiosa Neonatorum"	15.00
Otis R. Bowen—"The History of the Practice of Obstetrics"	15.00
Edgar A. Thompson—"Blood Transfusion"	15.00

Alpha Omega Alpha

The following members of the class of 1940 at Washington University School of Medicine, St. Louis, were elected to the Alpha chapter in Missouri of Alpha Omega Alpha: Russell J. Crider, Robert E. Buck, Perry C. Gillette, Horace M. Wiley, Seymour Brown, Richard L. Landau, Mary C. McFayden, Paul Guggenheim, Benjamin Strehlman, Wallace Rindskopf Jr., Llewellyn Sale Jr. and Leabert R. Fernandez. The following members of the class of 1941 were also elected at this meeting: Henry S. Guterman, Leon Kahn and Earl W. Sutherland Jr.

Temple University

The freshman class at Temple University School of Medicine, Philadelphia, gave its annual dance February 9 in Mitten Hall in honor of the sophomore class. The special guests on this occasion were the junior and senior classes, Dr. and Mrs. Earl A. Schrader, Dr. and Mrs. Robert H. Hamilton Jr. and Dr. Philena Chase. The favors were mother-of-pearl lavalieres with the medical school insignia superimposed.——Dr. Virgil H. Moon, professor of pathology at Jefferson Medical College of Philadelphia, addressed the sophomore class recently on "Shock: Its Mechanism and Pathology." The entire student body was addressed by Dr. Gilbert Dalldorf, chief of laboratories at Grasslands Hospital, Valhalla, N. Y., on "The Clinical and Pathological Evaluation of the Vitamins."——The Babcock Surgical Society has elected John B. Roxby Jr. '41 as secretary-treasurer; next year Mr. Roxby will succeed to the presidency. Student papers were read before the society January 11 by George Shugert '40 on "Primary Tumors of the Lung" and by Joseph Reno '41 on "Cryptorchism"; J. Guy Butters '41 and Joseph R. Connelly '40 read papers before the society, February 14, on "Treatment of Varicose Veins" and "Intercostal Neuralgia," respectively.——The basketball team at Temple University School of Medicine—Jack Moore, Robert Deen, Frederick Reese, Chauncey McGeorge, Norman MacKenzie, Sidney Sedwick, Taras Rybachok, Murray Sigman and Frank Viggiano—has won its fourteenth consecutive game, the recent victims having been Glassboro State Teachers College Alumni, the Temple University football team, and Temple University hospital interns.

Expenses at Long Island in 1940

The secretary for student employment at Long Island College of Medicine, Brooklyn, Dr. Milton B. Handelsman, sent questionnaires to all students at the college regarding their expenses, sources of income and financial difficulties, and 86 per cent of them were returned answered. From these data, the average estimated budget for the present school year for students living at home is from $1,035 to $1,135; for those boarding near the school the estimate is from $1,390 to $1,490. If scholarships were available to cover the cost of tuition, a student living at home would require only an additional $425, and a student boarding near school $780. Among the expenses listed in the average budget were tuition $610, books and instruments $100, clothing and the like $100, room $180, food $250, travel expenses $150, recreation from $50 to $100, incidentals from $25 to $50, and medical and dental fees from $10 to $25.

The data showed that the chief sources of income of 50 per cent of the students were from their parents; however, 14.8 per cent of the seniors, 8 per cent of the juniors, 10.5 per cent of the sophomores and 3.5 per cent of the freshmen were entirely independent of parental assistance. Of the seniors receiving parental support, 58.5 per cent felt that their studies imposed a severe strain on the family finances; of the juniors, 54 per cent; of the sophomores, 37.7 per cent, and of the freshmen, 26.4 per cent. There were many other sources of income; 16.7 per cent of the seniors worked during the school year, about 26 per cent of both the juniors and the sophomores, and 10.3 per cent of the freshmen. Twenty-four per cent of the seniors were

relying on repayable loans, about 12 per cent of the juniors, 15 per cent of the sophomores and 12.7 per cent of the freshmen. Personal savings accounted for the incomes of 16.7 per cent of the seniors and of 21, 15.1, 8.1 of the other classes, respectively. One and nine-tenths per cent of the seniors relied on their spouses for their income, 1.3 per cent of the juniors and 1.2 per cent each of the sophomores and freshmen. The usual amount earned by students performing small jobs through the school year varied from $150 to $200. The students who worked during the summer earned on the average a maximum of $250. With the exception of the freshmen, more than 50 per cent of the students expressed a desire to obtain some remunerative work. Such positions as policemen, chauffeurs, hotel clerks, lifeguards, laboratory assistants, playground directors, counselors in camps, illustrators and seamen were filled by the students who were employed.

Harvard Students in Peru

Henry F. Allen, William P. Carter, Calvin H. Plimpton, Calderon Howe and Ben Eiseman, all of the class of 1943 of Harvard Medical School, Boston, have just returned from Lima, Peru, where, under the direction of the Institute of Public Health, they completed during the summer a survey of the diseases of the rural population, the most prevalent of which were said to be leishmaniasis, oroya fever and verruca peruana.

Prizes Awarded at Colorado

The following prizes were recently awarded to students at the University of Colorado School of Medicine, Denver: Miss Dorothy J. Clark, '42, received the 1940 Chester H. Elliott Memorial Prize in pathology, amounting to about $30, for showing the greatest proficiency in the second year courses in pathology. Robert S. Redwine, '43, received the 1940 Alpha Omega Alpha Prize of $25 in anatomy, the winner having been designated by the faculty of that department. Miss Winifred M. Riggs, '41, was awarded the Carbon Gillaspie Memorial Prize of $25 in applied anatomy for having shown exceptional scholarship and technical skill in the course in that department. Robert W. Rasor, '41, and Chester P. Stevenson, '41, received the 1940 $10 prize offered by Dr. John G. Ryan for the best case report prepared by a senior or junior student.

Pennsylvania State Board Questions

The following questions were given by the Pennsylvania State Board of Medical Education and Licensure at the examination in Harrisburg, July 10, 1940:

GYNECOLOGY AND OBSTETRICS

1. Outline the management of the second stage of labor.
2. Discuss the treatment of pregnancy when complicated by essential hypertension and appearing in the first trimester.
3. Given a symmetrical pelvis with a diagonal conjugate diameter of 10.5 cm., how would you determine the proper management when the patient is at term?
4. Differentiate "retained placenta" from "adherent placenta"; outline treatment in a case of retained placenta.
5. Give the clinical course of a case of pernicious vomiting of pregnancy. What are the salient points in its treatment?
6. How will you diagnose and treat a case of infected incomplete abortion?
7. In a woman 30 years of age, what symptoms would occur from a retrocessed uterus, and how would you diagnose this condition? Detail one method of treatment.
8. What are the most frequent causes of postmenopausal uterine bleeding? Select one and give its diagnosis and treatment.
9. Give the differentiated diagnosis of four conditions which may cause enlargement of the abdomen in a woman 40 years of age.
10. What are the clinical aspects of trichomonas infestation of the vagina? Differentiate this from other types of vaginitis.

Prizes Awarded at Western Reserve

Gerald T. Kent, '40, a graduate of Western Reserve University School of Medicine, Cleveland, has been selected by the faculty of the school for the Charles F. Hoover Scholarship for 1940 in recognition of his outstanding scholastic record. Dr. Kent will serve as assistant in pathology until February, when he will take up his duties as intern in medicine at the University Hospitals.——The annual Alpha Omega Alpha awards have been made as follows: first prize to Robert E. Eckardt, '43, for his paper on "Vitamin B_6, Its Isolation, Synthesis and Physiology"; second prize to Daniel A. Brody, '40, for his paper on "Physical Factors in Gastric Evacuation"; third prize to John M. Cook, '40, for his paper on "A Study of Carbohydrate Digestion."——Samuel R. Ziegler, '40, was awarded the senior prize in obstetrics, the gift of Dr. Edwin C. Garvin; Jac Sidney Geller, '40, was awarded the senior prize in surgery, the gift of Dr. Elliott C. Cutler, and Eugene R. K. Leiter, '43, was awarded the Herbert S. Steuer Memorial Award for special work in anatomy.

Dr. Alvarez Gives McCoy Lecture

The students in New Orleans medical schools and the interns at Charity Hospital were invited to the inaugural lecture of the George W. McCoy lectureship, given at the Jung Hotel, March 26, by Dr. Walter C. Alvarez, of the Mayo Clinic, Rochester, Minn., on "The Origins of Modern Medicine." This annual lecture has been established by the Phi Beta Pi fraternity in honor of Dr. George W. McCoy, for many years a prominent officer in the U. S. Public Health Service and recently also professor of preventive medicine and public health at Louisiana State University School of Medicine. Dr. McCoy is a member of the Council on Pharmacy and Chemistry of the American Medical Association, of the National Board of Medical Examiners, of the Permanent Standards Commission of the Health Section of the League of Nations and of many scientific societies. He was awarded the Sedgwick Medal of the American Public Health Association in 1921.

Vanderbilt Sophomores Elected to Honorary Society

The Vanderbilt sophomore medical students elected to the local chapter of Alpha Omicron Alpha, national honorary medical fraternity, this year were John R. Hilsenbeck, Charles L. Cogbill Jr. and James H. Baxter. Only three members of the sophomore class are taken into this honorary fraternity each year, membership in which is based on scholarship and character.

Maryland's Recreation Center

The completion of the spacious Frank C. Bressler Research Laboratory has provided two floors in the Gray Laboratory Building which have been given over to the students for a lounge and recreation center. The students have enjoyed a program of medical motion pictures, lectures and the first student body dance in many years.

Undergraduate Honor Society at Louisiana

Announcement has been made of the formation of The Circle, an undergraduate honor society in the Louisiana State University School of Medicine, New Orleans, under the sponsorship of a faculty committee consisting of Drs. B. I. Burns, dean, Charles Midlo and James D. Rives. The fourth year membership is limited to the upper tenth of the senior class, and the third year membership to the three highest ranking students in the junior class.

Iowa Student-Faculty "Mixers"

Two committees have been appointed independently at the State University of Iowa College of Medicine to bring the students and faculty members together in activities of a social and cultural nature. The Student Council comprises one of these committees and the chairman of the other is Helen L. Dawson, Ph.D. Last year the two committees carried out similar programs providing for special speakers, movies and music, followed by a longer interval of good fellowship, with refreshments. The highlights of these programs were "Colored Movies of Old Mexico," made by Dr. Nathaniel G. Alcock; a talk by Dr. William D. Paul on "American Pattern Glass," a hobby; "Tall Tales of the Mississippi," by William J. Petersen, Ph.D., of the history department, and an amusing and scientific discussion of "Foulk's Law as a Basis for Predicting Postcurricular Achievement," by Col. J. J. Hinman. One of the most popular programs was a "Professor Quizz," in which a team of students and a team of faculty members opposed each other and for which the student prize was won by John M. Rhodes and the faculty prize by Walter R. Ingram, Ph.D.

Syracuse Personals

Edward M. Nutting, '41, of Syracuse University College of Medicine, Syracuse, N. Y., lost his life this summer by drowning.——Miss Mary Elisabeth Herberich, a senior, has been awarded the Dr. Menzo W. Herriman Scholarship, a full tuition award which is given annually to one of the five highest ranking students in the senior class. Miss Herberich is the first woman student to receive this award.——Six of the forty-eight new freshmen medical students at Syracuse this fall are sons of physicians. The class also includes three women.

Dance to Aid Students

The annual dance of the students of Long Island College of Medicine, Brooklyn, cleared about $400, which was turned over to the Student Loan Fund.

Tufts Freshmen Awarded Commonwealth Scholarships

The Commonwealth Fund has awarded scholarships to four students who will enter Tufts College Medical School, Boston, this fall as freshmen. Each of the four recipients will receive $1,000 for each of his four years of medical training, but he must agree to practice in a rural community in his home state at least three years following his internship. The scholarships have been awarded to C. Clark Streeter, West Somerville, Mass.; Clarence W. Whittaker, Easton, Maine; Frank E. Perron Jr., Manchester, N. H., and Theodore W. Ling, St. Johnsbury, Vt. All four recipients have B.S. degrees.

Prizes Awarded to Tulane Students

The dean of Tulane University of Louisiana School of Medicine, New Orleans, Dr. Maxwell E. Lapham, announced the following list of prizes and honors awarded to some of the 1940 graduates: William H. Harris Jr., a gold medal for the highest combination average in the four year course in medicine. This is the Isadore Dyer Memorial Medical Scholarship Prize. Stephen L. Stigler, the Sidney K. Simon Prize of $50 for his essay entitled "Vitamin K." A similar prize was awarded to Charles J. Edwards Jr. for his thesis "Alcoholism and Vitamin Deficiency." Mayo L. Emory and John J. Christian were awarded copies of Musser's book on internal medicine for the best theses in medicine. Edward B. Ferguson Jr., of the freshman class, was awarded the biochemical scholarship cup in the annual competitive oral examination.

Colorado Juniors Give Psychiatric Plays

The junior class at the University of Colorado School of Medicine, Denver, gives an amateur play each year dramatizing some psychiatric problem or situation. The plays are produced, acted and directed by members of the class, and the costs are underwritten by Dr. Franklin Ebaugh, professor of psychiatry. The last production, entitled "Doctor, Feel My Pulse," dealt with a family situation in which a mother-in-law and a timid husband make a young wife's life miserable. The family physician recommends calling in a psychiatrist, who endeavors to resolve the family problems by showing the wife how to use her wits, the husband how to become more masculine and the mother-in-law how to be less domineering. The play was directed by John Amesse, '41, and the parts in the order of mention here were taken by Winifred M. Riggs, '41, Claude O. Roberts, '41, Mary Barker, a student nurse, Howard Hamlin, '41, and John Benwell, '41.

Ohio Personal

Howard J. Scott, a senior at Ohio State University College of Medicine, Columbus, is the recipient of the first award from the Comly-Coleman Scholarship Fund, which provides for a full year's tuition. Our correspondent writes: "Because of 'Scotty's' sincere and indomitable spirit, his selection will be greeted by the hearty approval of his classmates."

Awards to Jefferson Students

At the 115th commencement of Jefferson Medical College of Philadelphia, June 7, the following students were awarded prizes:

Alan M. Schaeffer received the Henry M. Phillips Prize of $75, awarded on recommendation of the professor of medicine to the graduate in his opinion the most worthy.

Harvey K. Mechanik, the Henry M. Phillips Prize of $75, awarded on recommendation of the professors of surgery to the graduate in their opinion most worthy.

William W. Kitchin, a gold medal, awarded by bequest of Dr. Francis W. Shain for the best essay on a subject pertaining to the practice of medicine.

James R. Herron Jr., a gold medal, awarded by bequest of Dr. Francis W. Shain for the best essay on a subject pertaining to surgery.

Theophilus H. Boysen III, $25 by Professor Brooke M. Anspach for the best examination and clinical report on gynecology.

Richard H. Saunders, $25, by Prof. Horace J. Williams for the best examination in otology.

George F. Lull Jr., a gold medal, for general excellence in clinical surgery, in memory of Francis T. Stewart.

Clyde A. Collins, $25, by Prof. Norris W. Vaux for the best examination in obstetrics.

Francis X. Bauer, $25, by Prof. Edward L. Bauer for the best examination in pediatrics.

Harvey K. Mechanik, $25, by Prof. Charles E. G. Shannon for the best examination in ophthalmology.

Thomas H. Auginbaugh Jr., $25, by Prof. Louis H. Clerf for general excellence in laryngology and bronchoscopy.

John L. Simon, $25, by Prof. Bernard J. Alpers for the best examination in neurology.

John C. Grier Jr., $25, by Clinical Prof. Baldwin L. Keyes for the best examination in psychiatry.

Richard L. Wagner, a gold medal, for the best examination in therapeutics.

Alan M. Schaeffer, the William Potter Memorial Prize awarded to a graduate attaining the highest general average in the final two years of the medical course.

Harvey K. Mechanik, a medal, awarded by the alumni association for the best general average gained in the examinations for the entire curriculum.

Thomas M. Scaricaciottoli, a gold medal, awarded by bequest of Dr. Francis W. Shain, open to undergraduates of the second year for the best essay or examination on a subject pertaining to physiology.

John A. Pfister, a gold medal, awarded on completion of the sophomore year to the student with the highest grade in anatomic subjects of the first two years.

Frank T. O'Brien, a gold medal, awarded by Prof. J. Parsons Schaeffer for the best thesis in the science of anatomy.

John L. Simon, the W. B. Saunders Company Prize for the best general examination at the end of the senior year.

Frederick B. Wagner Jr., the D. Appleton-Century Company Prize for the best general examination at the end of the junior year.

Tulane's Quiz in Biochemistry

Edward B. Ferguson Jr., '43, Tulane University of Louisiana School of Medicine, New Orleans, who was named winner of the annual biochemistry oral quiz, will be presented with a book and a loving cup to be held for one year. The ten students having the highest average in the biochemistry class are eligible for the quiz, which questions are asked by the entire biochemistry staff. William D. Davis Jr., '43, was named runner-up.

Iowa Personals

The annual Baldridge-Beye Memorial Prize of $100 for original scientific work at the State University of Iowa College of Medicine was awarded to Albert P. McKee, '41.——Byron H. Evans and Dwight Sattler were awarded associate membership in Sigma Xi on the basis of scholastic excellence and original research. ——The following medical students were elected to membership in Alpha Omega Alpha during the last year: Forest H. Coulson, Byron H. Evans, Robert H. Foss, John H. Laubscher, Frederic G. Loomis, John J. Maloney Jr., Robert C. Miller, James W. Standeven, Thomas F. Thornton Jr., George I. Tice, Charles A. Waterbury Jr., John M. Rhodes, Margaret L. Vanderwilt, Samuel V. Thompson and Henry E. Hamilton.

Senior Awards at California

In the award of the annual Guy K. Woodward competition for fourth year medical students at the University of California, San Francisco, the first prize of $150 went to Julian S. Davis of San Francisco for his paper on "Coronary Occlusion with Special Reference to the Electrocardiographic Changes"; the second prize to Theodore E. Diller, San Francisco, for his paper on pellagra, and the third prize to Robert W. Godwin, Long Beach, Calif., for his paper on Ménière's disease. Milton Gordon, San Francisco, and Harry Levitt, Los Angeles, were given honorable mention. The awards were presented by Dr. William J. Kerr, professor of medicine.

Guest Lectures at St. Louis

Dr. Paul S. Barker, assistant professor of internal medicine, University of Michigan School of Medicine, Ann Arbor, addressed the junior and senior classes of St. Louis University School of Medicine at a special lecture on "Heart Disease in Pregancy."——Dr. Robert S. Berghoff, professor of clinical medicine, Loyola University School of Medicine, Chicago, lectured at a seminar, April 24, on "Senile Ectasy." The lecture was sponsored by Alpha Omega Alpha.

Emory A. O. A. Members

At a dinner meeting in May, Emory University chapter of Alpha Omega Alpha honorary medical society at Atlanta, Ga., initiated the following new student members: Julian C. Pate, Tampa, Fla., John Ranson Lewis Jr., Louisville, Ga., and George L. Beale, Cairo, Ga. Following the dinner, the annual Alpha Omega Alpha lecture was presented by Dr. Virgil P. Sydenstricker, professor of medicine at the University of Georgia School of Medicine.

Virginia Personal

Dr. Reginald Fitz, Harvard Medical School, Boston, was the speaker at the commencement closing the one hundred and second session of the Medical College of Virginia, Richmond, June 4. There were sixty-eight candidates for graduation in medicine.

Premedical Club at Ohio State

Ohio State University's premedical club was formally installed, May 31, as a chapter of Alpha Epsilon Delta, national premedical fraternity, at which twenty-nine students and four faculty members were inducted as charter members. Honorary members of the charter group are Dr. H. E. Setterfield, associate professor of anatomy, and Dr. Raymond J. Seymour, professor of physiology at the college of medicine. The installation dinner was held in the Pomerene Hotel, with Emmett B. Carmichael, Ph.D., national councilor of the fraternity and a faculty member at the University of Alabama, as the installing officer. Following the dinner, the fraternity sponsored an open meeting. Membership is limited to juniors or seniors who have a cumulative average of B in all studies. Alpha Epsilon Delta which was founded at the University of Alabama in 1926 now has twenty-nine chapters. It was first limited to men, but since 1929 has been open to women also.

The Bel Award at Louisiana

Dr. James T. Nix Jr., '40, Louisiana State University School of Medicine, New Orleans, received the George S. Bel Memorial Award of $50, which was given for the first time this year. The winner was selected by a committee of the faculty from the ten highest ranking students. Mrs. Bel stipulated that the award should be presented to the senior student who "symbolizes the highest ideals of medicine"; the prize was established in memory of her husband, the late Dr. George S. Bel, who was director of the department of medicine for many years.

Howard College

Dr. Louise H. Branscomb, Birmingham, Ala., addressed the twelfth annual founders' day banquet of the Howard College chapter of the Alpha Epsilon Delta honorary premedical fraternity, May 15, on "Women in Medicine."

"DO YOU KNOW WHAT PHYSICIAN"

Following are answers to the questions appearing on page 1145:

1. Dr. Joseph Warren of Boston, an ardent patriot. Dr. Warren had a high reputation as a physician and was retained by John Adams, who was later president of the United States, as his family physician.

2. Dr. Richard J. Gatling, who graduated from Ohio Medical College in 1850, after having become interested in the study of medicine through an attack of smallpox. He was born in North Carolina and was for some time a practitioner of medicine in Indianapolis. Dr. Gatling died in New York, Feb. 26, 1903, after the Gatling gun had been adopted by almost every great nation in the world.

3. Dr. Georges Clemenceau, who practiced medicine in New York and later in Paris as a dermatologist.

4. Dr. John McCrae of Montreal, Canada, who was lecturer in pathology and internal medicine at McGill University and formerly professor of general and special pathology at the University of Vermont, Burlington. Dr. McCrae was killed in service during the first World War.

5. Dr. Timothy Bright, who graduated in medicine at Cambridge, England, in 1574. His system had an alphabetical basis using the initial of each word.

6. Arthur Conan Doyle, who received his M.D. degree from Edinburgh in 1885. He was knighted in 1902.

7. Sun Yat-sen, who graduated from the College of Medicine in Hong Kong in 1892.

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